ANNALS OF SURGERY

VOL. 105 MARCH, 1937 No. 3

SYMPOSIUM
ON
THE INJECTION TREATMENT OF HERNIA
AT
THE UNIVERSITY OF MINNESOTA
MINNEAPOLIS, MINN.

THE STATUS OF THE INJECTION TREATMENT OF HERNIA.
OWEN H. WANGENSTEEN, M.D.

THE AMBULANT TREATMENT OF HERNIA.
ARTHUR F. BRATRUD, M.D.

AN EVALUATION OF THE RESULTS OF THE INJECTION TREATMENT OF INGUINAL HERNIA.
FRANK S. MCKINNEY, M.D.

THE INJECTION TREATMENT OF HERNIA.
CARL O. RICE, M.D.

STERILITY FOLLOWING THE INJECTION TREATMENT OF HERNIA.
CHARLES E. REA, M.D.

THE STATUS OF THE INJECTION TREATMENT OF HERNIA

Owen H. Wangensteen, M.D.

Minneapolis, Minn.

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MINN.

The injection method of treating herniae which is now almost a century old has been revived within recent years. In France this plan of dealing with inguinal hernia was developed by Velpeau[4] following the designing of the hypodermic needle and its introduction into medical practice. In this country, this management of hernia was advocated by Heaton[3] and Warren.[5] The latter wrote a treatise upon the subject in 1881. This was eight years before an adequate operative technic for the cure of hernia had been worked out in the hands of Bassini[1] and Halsted.[2] Had the principles of asepsis and the necessity for their rigid exercise been as well understood in 1881 as they were in 1889, it is not unlikely that the nonoperative treatment of certain types of hernia would have found earlier acceptance. The rapidity with which surgical measures in that period were applied to a great number of disorders has become familiar to all who have a reading acquaintance with the development of surgical procedures and technics.

The injection treatment of hernia was introduced into the surgical clinic of the University Hospital by Dr. A. F. Bratrud in 1931. Its employment has since continued here in the hands of a small group. Dr. C. O. Rice of this department, with the permission of Dr. A. A. Zierold, Chief of the Surgical Staff at the Minneapolis General Hospital, instituted this nonoperative method of dealing with selected herniae there. Anyone who manipulates a novel or new therapeutic measure in medicine owes an obligation to the profession to report his unprejudiced appraisal of its merit. In the years which have intervened since the injection method of dealing with herniae was first used in the departmental surgical outpatient clinics, certain impressions have been formulated concerning the frailties and virtues of the method. It is the purpose of the accompanying papers to relate those experiences.

It has been found that a large proportion of the patients with indirect inguinal hernia who report to these two outpatient surgical teaching clinics of the University of Minnesota can be dealt with satisfactorily in the ambulatory fashion described in the papers by Drs. Bratrud, McKinney, and Rice. It is important, as they point out, that the surgeon have the full cooperation of the patient. It is also apparent that only *reducible* herniae are suitable for injection; proper retention of the hernia by a suitable truss is mandatory *before* the injections are instituted. The selection of *appropriate* cases is extremely important. The small reducible, indirect inguinal hernia in the young person with strong tissues seems most suitable for this method of

---

Submitted for publication October 8, 1936.

treatment. An anxiety to extend the method to cases that present large defects and poor tissues results in a large incidence of failures. It would appear likely that the cure of hernia effected by parasaccular injection will be followed by a somewhat higher incidence of late recurrence than after the operative method in which hernioplasty is also done in addition to obliterating the hernial sac. Satisfactory results have been obtained in some direct herniae as well as in isolated instances of patients with femoral, umbilical, and epigastric herniae.

It is generally admitted that the operative treatment of hernia is only to be assumed by those who possess an adequate acquaintance with surgical technic and knowledge of the anatomy of the abdominal wall. He who undertakes the injection method of treating inguinal hernia should possess ready familiarity with the anatomy of this region. The injection of sclerosing solutions into the abdominal wall by persons not well oriented in the surgical anatomy of the groin or not possessed of an intimate knowledge of the technic of the method is as *hazardous* as the operative method in hands which have not been trained. Skill is as important a determinant for success with the employment of this method as it is in the operative treatment of hernia. Unwarranted zeal on the part of enthusiasts of the injection method of dealing with hernia to extend its use to cases which are obviously not suitable or amenable to cure by this means will not only retard its acceptance by the profession, but will serve to discredit the method as much as its employment by unqualified persons.

The method, like any operative procedure, is not free from complications even in practiced hands as the accompanying papers attest. It is not without significance, however, that not one patient of the several hundred treated by this method in the two surgical clinics has died as a direct result of the treatment. As much can rarely be said for large series of similar size treated by operation. This method of treating selected cases of hernia has merit and when skilfully employed would appear to carry little risk of serious complication.

Medicine has come to recognize the superiority of trial over reason. Rationalizations concerning the merits of a method are likely to lead to error, not so much because the logic employed is poor but more often because the initial premise itself is false. The injection treatment of hernia is not therefore to be dismissed without examination. The rejection of obliteration of hemorrhoidal varicosities and varicose veins of the lower extremity by injection is fresh enough in the recollection of medical men to remind them that prejudices cannot delay the march of progress.

Time will ultimately judge impartially of the merits of the injection method of treating herniae. Surgeons are, I believe, not more objective than any other group of medical men. They know well the anxiety that the contemplation of an anesthetic and an operation provokes in the minds of most patients. When the question of the best sclerosing agent has been settled and the technic of the procedure has become better standardized, and when sufficient trial in practiced hands has adequately shown that selected herniae can be satisfactorily treated by injection without recourse to operation, surgeons generally will probably welcome this means as a valuable addition to acceptable methods of dealing with hernia.

REFERENCES

[1] Bassini, E.: Ueber die Behandlung des Leistenbruches. Arch. f. klin. Chir., **40**, 429, 1890.

[2] Halsted, W. S.: Radical Cure of Inguinal Hernia. Bull. Johns Hopkins Hosp., **1**, 12, 1889.

[3] Heaton, G.: The Cure of Rupture, Reducible and Irreducible. J. H. Davenport, Editor. Houghton, 1877.

[4] Velpeau, A. A. L. M.: New Elements of Operative Surgery. Translated by P. S. Townsend. **3**, 554. New York, Wood, 1847.

[5] Warren, J. H.: A Practical Treatise on Hernia. Boston, J. R. Osgood & Co., 1882.

THE AMBULANT TREATMENT OF HERNIA

ARTHUR F. BRATRUD, M.D.

MINNEAPOLIS, MINN.

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MINN.

INTEREST has been manifested at various times in the past concerning the ambulant treatment of hernia, but it has never become popular. As early as 1880, Billroth made the statement that if anyone could obtain a solution that would cause the artificial proliferation of tissue that would be as dense and tough as fascia, the radical cure of hernia would be solved. Apparently Velpeau,[18] of Paris, must be given the credit for being the first surgeon to use irritants with the idea of producing a proliferation of new connective tissue to obliterate the sac of an inguinal hernia. He reported several cases as being successfully treated by the injection method. In 1842, Heaton,[7] in Boston, treated a few cases by the use of tincture of iodine. It was not until 1877 that he published a book describing his treatment. Due to the fact that Heaton would not divulge the exact technic to the medical profession, his work never received official recognition. After the publication of Heaton's book, Warren,[19] of Boston, who was associated with Heaton, later published a book on the Treatment of Hernia. Other men who contributed to the early literature should be mentioned, notably Schwalbe, Janney, Lannelongue,[10] Ripley, Coe, McDonald, and Mayer.[11] On account of the numerous complications and the fact that the work was not performed by able surgeons, the treatment received a great deal of criticism.

During the past five years the writer has endeavored to perfect a method to cure certain herniae by the injection of sclerosing solutions. The purpose of this paper is to present the results of animal experiments as well as the

---

Submitted for publication October 8, 1936.

clinical impressions and results obtained from the application of the method to outpatients.

EXPERIMENTAL WORK.—Various solutions have been employed in experimental work on dogs and rabbits, as well as in the treatment of herniae in patients. The formulae for solutions which the writer has used to date are as follows:

Phenol-Thuja Mixture:

Phenol	50 parts
Alcohol	25 parts
Lloyd's specific tincture of thuja	25 parts

Allow to stand two days and then either decant or filter.

Mayer's Solution:

Zinc sulphate	1 dr.
Phenol crystals	6 dr.
Glycerin	4 fl. dr.
Aq. cinnamomi	1 fl. oz.
Fl. ext. pinus canadensis (dark)	5 fl. dr.
Sterilized chemically pure redistilled water	2 fl. oz.

Dissolve the zinc sulphate in the cinnamon water. Liquefy the phenol crystals by heating. Add the glycerin. Shake thoroughly until mixed and cooled; then add the distilled water and finally the fluid extract of pinus canadensis. Shake thoroughly. Allow the fluid to stand for about a week, agitating the mixture several times a day. Subsequently it should be filtered. Before injecting, boil the solution in a glass tube.

Other solutions which have been used in experimental work are oleic acid, quinine urea, in strength up to 3 per cent, Pina Mestre solution, Proliferol, which is a distillate of several botanical drugs to which have been added tannic acid, benzol alcohol and thymol in various strengths up to 1 per cent, allantoin, cystein, ethereal oil of thuja, fluid extract pinus canadensis in strengths of 1, 3 and 10 per cent, and psyllium seed extract.

For the experimental work various solutions in quantities of three minims up to 3 cc. were injected below the fascia of the rectus abdominis muscle as well as into the abdominal cavity and subperitoneal tissue of dogs and rabbits. Injections were made about twice a week. A few solutions produced no proliferation at all while other solutions produced a marked proliferation of fibroblastic tissue. When the phenol-thuja mixture, Proliferol, Pina Mestre solution, Mayer's solution, or ricinoleate solutions were used, the tissues showed marked induration and thickening. All tissues showed an early necrosis before fibroblasts appeared which permeated the muscle fibers. This, according to Dr. E. T. Bell, Professor of Pathology at the University of Minnesota, "Produced a binding effect." There was no late infiltration of polymorphonuclear cells, or any evidence of late necrosis. A few days after the injection of the solution there was an infiltration of polymorphonuclear cells with necrosis varying according to the strength of the solution used. Fat necrosis was present in the muscle when ricinoleate solutions were used. When the solution was injected into the peritoneal cavity, the omentum became very adherent at the site of injection, the fibroblastic tissue having completely obliterated the peritoneum. Loops of bowel were very adherent, but no obstruction was present. Pina Mestre solution produced necrosis which seemed sufficient to contraindicate its clinical use. With the original Pina Mestre solution there was found a marked proliferation of fibroblastic tissue with foreign body giant cells. A solution consisting of a distillate of the tinctures reported to be in the formula for the original Pina Mestre solution was used. To this was added tannic acid in standardized strengths, varying from 0.15 to 1 per cent, as well as thymol 0.5 per cent and benzol alcohol 3 per cent. This produced a marked proliferation of fibroblastic tissue. The proliferation did not begin as early as that following the injection of the phenol-thuja mixture, which could be seen as early as the fourth day. A number of dogs were injected with fluid extract pinus canadensis in alcohol and phenol, in strengths of 1, 3, and 10 per cent. These are the basic drugs in Mayer's solution. They produced necrosis, abscess, and in one dog, peritonitis and death. The proliferation of fibroblastic tissue is more marked than in the specimens following the injection of the distillate mixture. No giant cells were found. Sections of tissues following the injection of tannic acid mixtures showed a dense fibrosis. Injection close to the peritoneum or just within the peritoneal cavity showed no evidence of abscess or necrosis, but a similar picture. The omentum was adherent to the abdominal wall, and there was so much proliferation of fibrous tissue as to completely obliterate the peritoneum. Results of injection below the fascia of dogs and rabbits showed a marked proliferation of fibroblastic tissue with no evidence of late necrosis, or infiltration of polymorphonuclear cells. However, polymorphonuclear cells are present when proliferation is first noticed, which is about the fourth day. Sections from dogs injected with the original Pina Mestre solution, as well as the distillate of the drugs contained in the formula, showed a reaction which could hardly be differentiated one from the other except that the section from the original Pina Mestre solution showed better developed foreign body giant cells. There was no late infiltration of polymorphonuclear cells or necrosis in these specimens. Injection of allantoin in strengths of 0.25 to 1 per cent, cystein 1 per cent, or oleic acid, produced no fibroblastic proliferation at all. Where psyllium seed extract was used, there was quite marked early necrosis as contrasted with the tannic acid preparations. There was very good fibroblastic proliferation, but there was late fat necrosis in the muscle tissues.

Before treating any patients, colored novocain solution was used to inject the internal inguinal ring, and it was surprising to note how the solution could be deposited around the internal inguinal ring with the technic to be described. The phenol-thuja solution was the first used. On account of the burning that resulted from the injection of an aqueous tannic acid preparation, various local anesthetics, novocain, nupercain, and benzol alcohol were employed. These diminished the burning pain, but a large percentage of these patients would have symptoms of an acute coryza on the following day. This did not occur in all cases, but in so many that it was discontinued. This was thought to be due to the fact that tannic acid did not exist in colloidal form in the synthetic preparation and was more rapidly absorbed, thus causing toxic symptoms. The histologic change in tissues of the treated patients is the same as that in injected animals. There is always an exudate which varies according to the strength of the solution used. There is more early necrosis with the phenol-thuja mixture than with any of the tannic acid mixtures. However, the fibroblastic tissue which results following the injection of the phenol-thuja mixture is denser and tougher than where tannic acid preparations are used.

Selection of Cases.—The injection treatment of hernia can be carried out in patients of all ages, provided that the hernia can be completely reduced and held completely reduced by a properly fitting truss during the period of active treatment. Umbilical, indirect inguinal, direct inguinal, and recurrent herniae give the best results. A few femoral herniae can be successfully treated by this method. Postoperative or incisional herniae usually have adhesions or incarcerated abdominal viscera and no definite sac, and should not, as a rule, be so treated. Incisional herniae usually have one hernia that can be diagnosed, but have several potential herniae along the line of the incision. If there has been a very small incision, if a definite opening can be determined, and if the contents can be reduced and held reduced by a properly fitting truss, this hernia can be so treated. Herniae associated with an undescended testicle, and incarcerated or irreducible herniae should not be 2
injected on account of the danger of strangulation. These are distinct surgical conditions. Herniae that can be reduced, but where the symptoms cannot be completely relieved by proper application of a truss, are unsuited for the injection treatment. Sliding herniae should not be so treated. It is very doubtful if a sliding hernia can be held reduced by a truss. Any general surgical contraindication, such as hyperthyroidism and hemophilia, should always be considered a contraindication. Large scrotal herniae give doubtful results, but these cases should be fitted with a truss both before being referred to surgery and after surgical repair. Laying aside the contraindications, it may be said that any inguinal hernia can be treated provided that it is reducible and can be held reduced by a properly fitting truss, and provided there are no surgical contraindications, as mentioned above. If there is any suggestion of an impulse or the hernia comes down occasionally after fitting of a truss, the case should be operated upon, not injected. Although a few femoral herniae have been treated with good results, I believe that there are liable to be complications, especially in large herniae. Several epigastric herniae have been treated with good results. Very often in femoral, umbilical or epigastric herniae, there is a fat pad in the sac. Application of a truss in these cases causes pain. These cases should not be treated unless there is absolute and complete relief of symptoms.

3

THE TRUSS.—It is absolutely necessary, primarily, to know how to fit a truss in order to keep the hernia reduced. By holding the hernia reduced the truss keeps the walls of the sac in direct apposition so that when fibroblastic tissue begins to form, the sac is completely obliterated by the new fibroblastic tissue. Should any abdominal viscera be retained within the sac it would be impossible to effect a cure, as any straining would force the contents farther down, separating the walls of the sac. Any type of truss can be used provided it holds the contents within the abdomen. For a single hernia a spring type of truss is more comfortable than a band type of truss (Fig. 1), for it does not have a tendency to move when the thighs are brought forward. A spring type of truss can be fitted to double herniae, although a band type of truss usually gives better results. For umbilical herniae, the best form of truss is a hard pad which fits into the hernial orifice and is held in place with an elastic bandage wrapped around the body several times. There should also be two thin plates which fit over the pad. The first plate should come to the inner edge of the rectus abdominis muscle, and the outer plate should come to the junction of the outer and median third of the muscle (Fig. 9b). This is a definite improvement over any previous truss or binder used for this type of hernia.

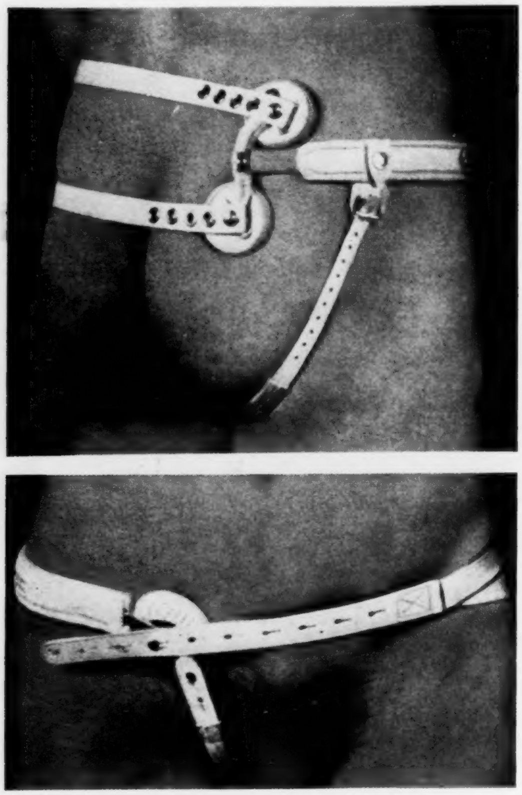
FIG. 1.—The spring type of truss used in the Hernia Clinic of the University of Minnesota Hospitals. Various types of pads can be fitted to these trusses, and this is of great importance. It is not always necessary to have a large truss pad for a large hernia.

Measurements for trusses are taken directly around the body at the level of the hernia, or 2 cm. below the crest of the ilium down to the symphysis pubis. Trusses should always be worn a sufficient length of time so that the soreness which results after first applying the truss has completely disappeared. With larger herniae it is advisable to wear the truss a longer period of time, even a month or six weeks, before starting treatment. Patients are advised to wear a truss both day and night during the period of treatment, and as long as one month after the period of treatment is over. An elastic truss is more comfortable while lying down than any other form. Trusses, when properly fitted, permit the patient to engage in almost any form of exercise or work. They are usually fitted too low, and when so fitted very often give relief, but do not hold the contents of the hernia reduced. They cause the hernial contents to press outward against the fascia of the external oblique, and a resultant fraying or thinning out of the fascia, as well as an enlargement of the defect in the transversalis fascia occurs. Very definite instructions should be given patients in regard to proper fitting and wearing of a truss, and especially with regard to the readjustment of the truss in the event of loss of weight.

TECHNIC OF PROCEDURE.—The technic for treatment where the phenol-thuja mixture or Mayer's solution is used, is to begin with two to five drops, injecting at the internal ring (Figs. 4 and 5). Not over eight minims should ever be used at one injection. Injections are made about twice a week, depending upon the reaction of the individual. Should there be much reaction, then the duration of time between the injections is lengthened. After several injections at the internal ring, there is usually sufficient plastic exudate so that the hernia does not come down, even when the truss is removed. Injections are also given at several points along the inguinal canal, just beneath the fascia (Fig. 6, needle A). Injections are also given just inside the external ring (Fig. 6, needle B), and also in Hesselbach's triangle (Fig. 7). For the injection of Hesselbach's triangle, the needle is introduced inside the cord and posterior to it, depositing the solution upon the conjoined tendon or the transversalis fascia.

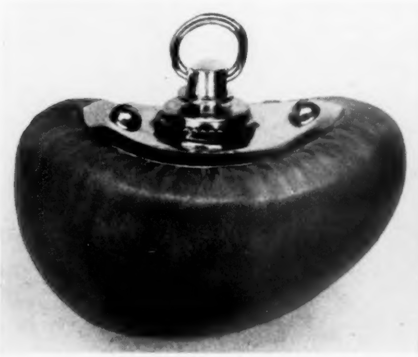

FIG. 2.—This type of pad is especially useful in indirect inguinal herniae, and in people who are very stout. The thick portion of the pad can be turned either upward or downward. For a direct hernia the thick portion of the pad should always be downward toward the pubis.

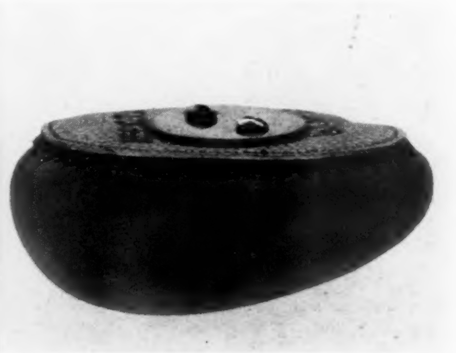

FIG. 3.—This type of pad is especially useful in stout individuals. One side of the pad is much thicker than the opposite side. Very often a hernia can be held with this type of pad on a truss where no other type of pad will hold. This is probably due to the fact that the thick portion of the pad fits along the shelving edge of Poupart's ligament. These pads can be fitted on to almost any band type of truss.

The number of injections required to close the hernia varies. A few cases have received only four treatments, and had a good result. As many as 20 injections have been given to cases with large scrotal herniae. It is much better to give more treatments than necessary and be sure of a good closure. There is more reaction or soreness with the phenol-thuja solution or Mayer's solution than with the Proliferol solution. However, the phenol-thuja solution produced more proliferation than the other solutions. With Proliferol, the treatment is started at the internal ring. No more than 2 or 3 cc. of the solution should be given at the first treatment, and where the stronger solutions of Proliferol are used, not over 3 to 5 cc. should be used at any time. Injections should also be made at the external ring and along the canal below the fascia so as to completely close the canal. Also Hesselbach's triangle should be treated in all indirect inguinal herniae, so as to protect against a direct hernia.

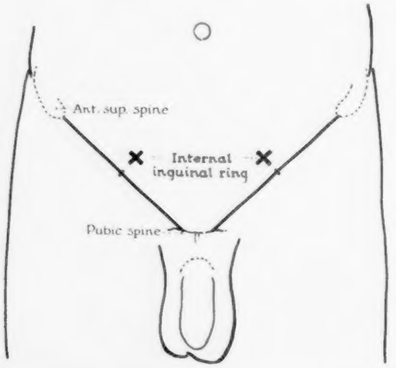

Fig. 4.—The location of the internal inguinal ring, which is approximately 1 cm. above the midpoint between the anterior superior spine of the ilium and the spine of the pubis. This varies according to the size of the hernia, so that in a very large inguinal hernia, where the defect in the transversalis fascia is greater, the ring will extend lower. This location is above the line between the two spines and not along the line.

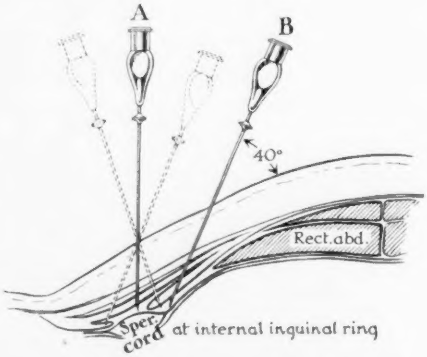

Fig. 5.—The injection of the internal inguinal ring. The needle A is introduced directly through the skin, fat and fascia of the external oblique muscle. As the needle penetrates the fascia, there is a distinct "give" feeling. Very little experience is needed to determine this location. As the needle is introduced slightly farther, depending upon the thickness of the abdominal wall, it will approach the region of the internal inguinal ring. When the needle is in the proper location, the syringe can be rotated in a circle, thus giving free rotation of the tip of the needle. This can be very easily demonstrated by the injection of colored novocain solution, preparatory to operating upon a hernia. If the needle touches the peritoneum, there will be marked pain as the parietal peritoneum is quite sensitive. The internal inguinal ring can also be injected by introducing the needle B at the lateral border of the rectus abdominis muscle, at an angle of approximately 40° to the skin, and penetrating until it meets the resistance of the transversalis fascia.

It is preferable to treat these cases twice weekly, although they can be treated daily with good results. There is much less after-pain or soreness with this solution than with the other solutions. The treatment should be continued until the entire inguinal canal is filled with a plastic exudate which becomes indurated and hard, and until no impulse occurs. It is not advisable to have the patient strain and cough until it is fairly certain that the hernia is obliterated. Occasionally there will be swelling of the cord, but this does not contraindicate treatment at that time. The swelling always subsides in a few weeks. In direct herniae the region of the internal inguinal ring should be injected to guard against development of an indirect hernia. Where there is a very large external ring, phenol-thuja solution is often used in combination with the distilled mixture. Here the region of the internal ring is injected with the distillate mixture and the phenol-thuja solution is injected at the external ring below the fascia. At the next treatment, the phenol-thuja solution is used at the internal ring, and the distillate mixture at the external ring. Only half the usual amount should be used when treating in this manner. About one treatment with the phenol-thuja mixture to three or four of the Proliferol seems to give better results than either one alone. At the present time it appears as though our best results follow the use of a combination of the phenol-thuja mixture with Proliferol. For this two drops of the phenol-thuja mixture are added to 1 cc. of Proliferol. Ricinoleate preparations very often cause severe after-pain or cramps and occasionally result in shock.

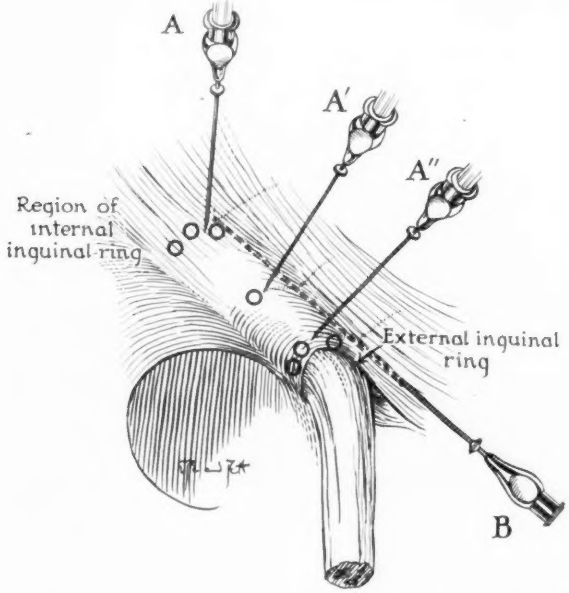

FIG. 6.—Various points of injection along the inguinal canal (needle A). The solution should always be deposited below and not superficial to the fascia of the external oblique muscle. Several points should be injected at the external ring. The needle point should be within the external ring so that none of the solution infiltrates into the subcutaneous fat. When this happens, a hard nodule will form. The needle should not go deep enough to injure the cord.

The internal ring can also be injected by introducing a 2½ or 3 in. needle (B) through the external ring, and passing it upward along the inguinal canal to the region of the internal inguinal ring. After passing the external ring it is carried upward to about 1½ to 1⅞ in. There is, however, more danger of injuring the cord with this technic.

An ordinary 5 cc. Luer syringe, with a 2 in. No. 22 gauge needle, is very satisfactory for the injection. An alcohol sponge for preparing the skin is sufficient as demonstrated by the few abscesses that have developed.

Before injection of the irritating solution, 2 cc. of 2 per cent novocain solution without adrenalin are injected at the site to be treated. The needle is left in place and in a minute the solution is injected into the anesthetized area. Aspiration should always be attempted before injecting any solution. Where the ricinoleate preparations or phenol-thuja mixture are used, it is not necessary to use any anesthetic. Up to 5 cc. of Proliferol can be used at a treatment. Up to 3 cc. of the ricinoleate solutions can be given at one treatment. Figures 8 and 9 show methods of injection of femoral and umbilical herniae.

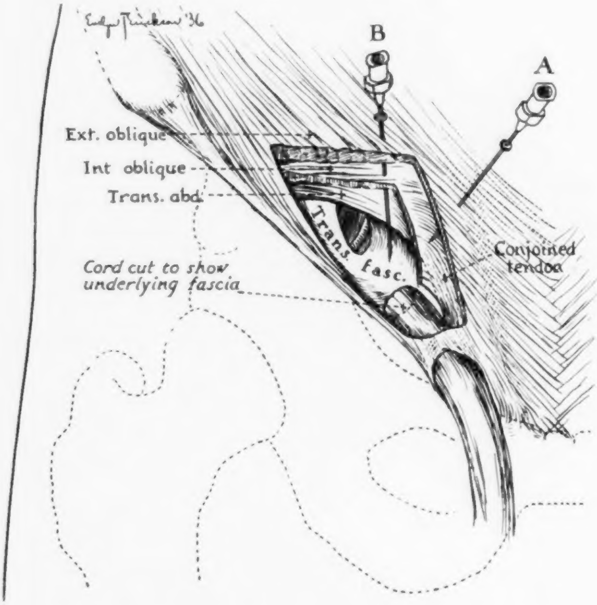

Fig. 7.—The technic for the injection of Hesselbach's triangle. In the case of direct herniae the needle (A) can be slid along the outer edge of the rectus abdominis muscle or can be inserted (B) into the triangle lateral to the rectus abdominis from above. In this manner the triangle can be injected without injury to the cord. The needle should be introduced until it meets the resistance of the transversalis fascia in the conjoined tendon.

Complications.—A number of complications have been mentioned: swelling of the cord, hydrocele, epididymitis, sepsis, strangulation, sterility, abscess, and peritonitis. Occasionally there will be a systemic reaction following the use of tannic acid preparations. This has not resulted since the use of synthetic tannic acid in alcohol was discontinued. With the ricinoleate preparations there is very often marked pain which may become general over the entire abdomen. This may be so severe as to simulate shock. Swelling of the cord has been noted in a few cases and this has usually appeared toward the end of the treatments, but has caused no serious disability. Only rarely can fluid be aspirated from an hydrocele of the cord. Where an hydrocele of the cord has resulted it will usually be absorbed and cause no serious trouble. Occasionally a case will show an anesthesia or hyperesthesia after treatment.

This will usually be confined to an area in the lower inguinal region, or the anterior surface of the thigh. One case had a temporary partial paralysis of the femoral nerve. He complained of weakness of the leg on standing, and the tendency of the leg to draw backward and upward. When seen one hour later this had completely disappeared, and he was working at his usual occupation in about three or four hours. Phenol-thuja solution was used in this case. There was, however, no permanent anesthesia, epicritic or protopathic. From correspondence with other physicians I have learned of three cases with similar reactions. In one of these there occurred a slight atrophy of the quadriceps femoris group of muscles. One case had an hyperesthesia of the thigh which lasted four weeks before clearing up completely. There have been two cases that developed abscesses and a slough, neither of which proved serious as the slough was entirely in the subcutaneous tissues. Two additional cases were seen in consultation that had been injected with phenol-thuja solution. Immediately after injection there was severe pain near the parumbilical point on the injected side. Discoloration of the skin and a slough resulted in these cases. This probably resulted from the injection of the mixture into the deep epigastric artery, causing complete obliteration of the terminal distribution of the epigastric artery so that the collateral anastomoses could not be reestablished before necrosis began. If the precaution had been

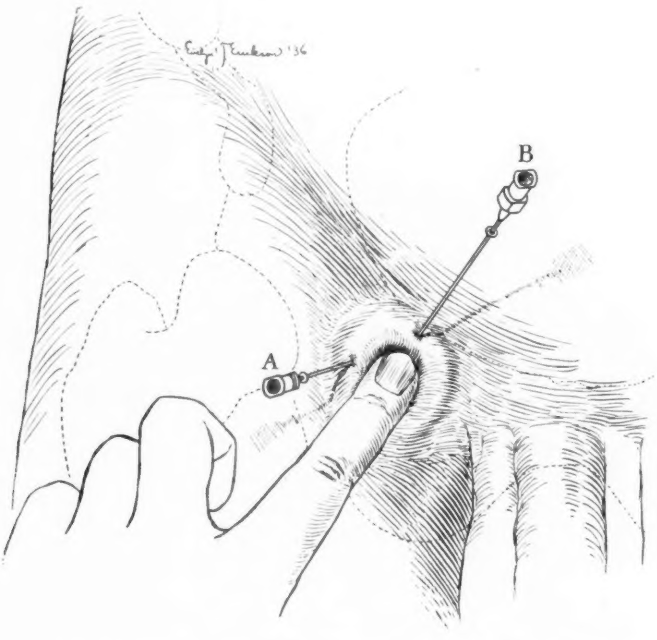

FIG. 8.—Femoral herniae can be injected very easily by placing the tip of the finger in the femoral canal, and then injecting the solution immediately below the tip of the finger. Not over two or three drops of phenol-thuja solution or 2 cc. of other solutions should be injected at one time in femoral herniae. As a rule, not over three or four injections are necessary to obliterate a femoral hernia.

observed of aspirating before injection this complication could have been obviated. There have been no cases of peritonitis in our own series of cases. One of our cases which was injected with Proliferol had very severe abdominal pain after treatment. He was operated upon immediately but showed no evidence of peritonitis or infection of any kind. The hernia was repaired and the postoperative course was uneventful. Occasionally a case will have pain as soon as the injection is commenced, regardless of whether it is below the fascia or in the deeper structures. If this happens the injection should be stopped. Such pain has proven temporary and has never continued for any great length of time. A few cases have had general abdominal pain, but without untoward effect. In the main such pain has lasted but a few minutes. In one instance, however, it continued for a day and it is my impression that the injection fluid entered the peritoneal cavity in this case. One case treated elsewhere died at the University Hospital. Sixteen minims of phenol-thuja

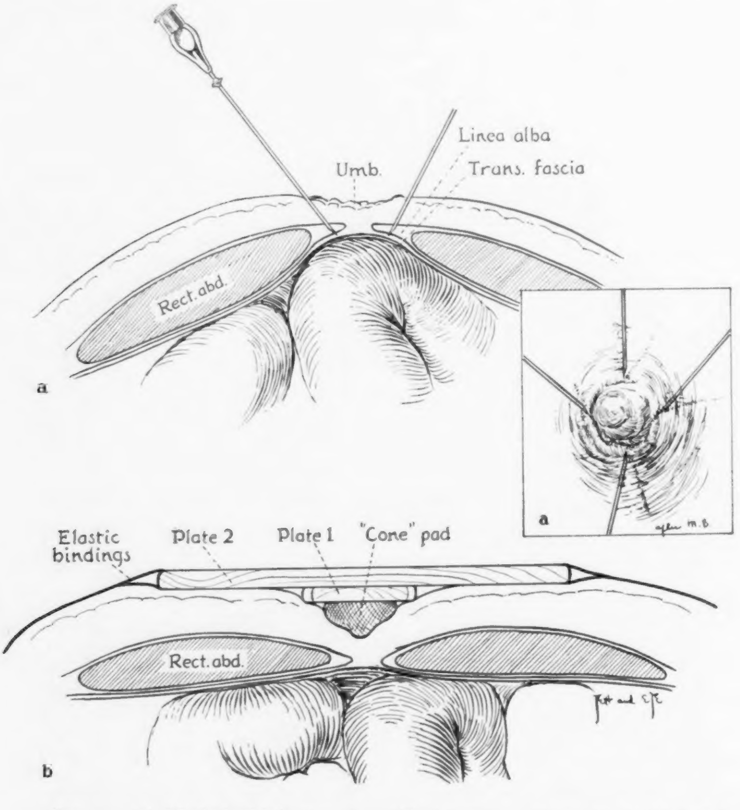

FIG. 9.—(a) Method of injection of umbilical herniae. Novocain should first be used as injected in inguinal herniae, only in a small quantity. Not over 1 to 1½ cc. of Proliferol should be injected at a time at various sides of the hernia. The needle should reach down to the edge of the fascia. (a′) Various points around the hernia should be infiltrated. (b) Cross section of an umbilical pad, showing cone-shaped truss pad which fits into the hernial opening and then two plates which support this. After this pad is put in place, it is held by an elastic bandage wrapped around the abdomen several times.

mixture had been injected into the peritoneal cavity with perforation of the ilium, resulting in peritonitis and death.

The course in cases treated after injection shows an induration in the region of the injection. This is usually tender to pressure on the day following treatment. Usually after two to four treatments there is sufficient exudate or plastic tissue formation to prevent protrusion of the viscera even without the truss. There have been a few cases where a swelling of the cord resulted, but this usually subsided in a few weeks. Hot packs relieve the pain when present. The external ring shrinks in size and the fascia can be felt to thicken, so that at the end of a few weeks the external ring will not admit the tip of the index finger. This usually begins after two injections at the external ring. Practically all patients mention the great relief obtained as soon as they are fitted with a truss and have had two or three treatments. There is less soreness and pain from Proliferol than from either the phenol-thuja or Mayer's solutions, and this, used in conjunction with the phenol-thuja solution, seems to give better and quicker results than any of the solutions alone.

Objections.—The objections which have been mentioned concerning this type of treatment should be considered. Paraffin injections can be dismissed without further discussion, for it is a well established fact that the method resulted in very few permanent cures. It caused irritation from the foreign body present, and required surgical interference for its removal and the closure of the hernia. The fact that it has been used only by quacks is not a good argument, for it is not so many years ago that reputable medical men were severely criticized for the injection of hemorrhoids or varicose veins, and today they are both accepted and recognized. The so called Timmerman treatment by alcohol should be discarded on account of the large number of injections required, and the fact that numerous complications have resulted. The fact that irritating solutions cause discomfort and pain sufficient to cause patients to be incapacitated has not been substantiated. It is true that some cases will have a greater reaction than others, but very few cases suffer sufficiently to incapacitate them from heavy work. Another objection is the fact that the truss must be worn for a long period of time. A properly fitting truss is of no more inconvenience than a well fitting glove, after the first few days. I think it can be safely stated that 80 per cent of all hernia cases are wearing trusses at the present time, and that only one out of ten trusses holds the hernia properly reduced. It has been stated that this is a blind and not a rational procedure. To that I may reply that there is a definite technic, and unless this is learned great harm may result. This cannot be too strongly emphasized.

Advantages.—There are several advantages in this form of treatment, the principal one being that it is ambulatory—the patient continues working, is not confined to the hospital for a period of two weeks, and is not incapacitated for another period of four to eight weeks. There is no question but that the economic issue is of greatest importance at the present time. To illustrate this, one case may be cited. It concerned a man 67 years of age, with a large scrotal hernia, suffering from a bronchial asthma and hypertension. He had had two recurrences following surgical repair, and was wearing the fourth ineffectively fitting truss. There was a large ulcer in the groin. This was a case of complete total permanent disability. He was put to bed with the foot of the bed elevated, and was given daily injections for five days. He returned to duty on the seventh day, and has continued at his employment without losing any more time. At the present time he has a very good result, but he has been advised to always wear his truss when he has a bronchial cough.

There is no question but that recurrences of hernia following surgery are much greater than statistics show, for herniae will recur, or a new hernia develop, as late as 15 to 18 years after the operation. It is most difficult to obtain satisfactory information concerning the actual percentage of recurrences. The incidence of recurrence following the injection treatment is really higher than stated by most men. A number of surgical cases that began to show weakening and beginning recurrence were fitted with a truss and treated by injection. In this manner recurrence of the hernia may be prevented. I believe that the recurrence of hernia following operation can be largely done away with, provided that patients are fitted with a truss and compelled to wear it for a period of time after operation. The case should be supplemented by injection treatment if there is any suggestion of recurrence.

DISADVANTAGES.—Among the disadvantages of this form of treatment should be mentioned the prolonged period of treatment; the wearing of a truss; inability to cure a small percentage of herniae, and the reaction which is manifested by pain and swelling which a few cases develop. However, where a truss fits properly it is not a discomfort. Very rarely does a case have such a severe reaction as to incapacitate him. There will be an occasional case which cannot be successfully treated, but this does not form any contraindication as far as later surgery is concerned.

These cases are not discharged as cured until they have been observed for at least one to two years. They are kept under treatment until a good firm induration is established throughout the inguinal canal, and there is no impulse on coughing or straining. Patients should not be made to cough or strain before at least six injections have been given, or before it is felt that the hernia is closed. A good method of determining whether or not the hernia is completely closed is to have the patient stand and, after straining, massage the inguinal region to determine whether any feeling of weakness or "give" can be felt.

INSTRUCTIONS TO PATIENTS.—The following instructions are given to every case concerning the essentials of treatment:

(1) The truss should be worn next to the body, removed in bed and put on in bed; the truss is to be worn night and day for a month after treatment is finished.

(2) If the truss does not stay in position, a strap fastened in front and back will hold it in place.

(3) The pressure of the pad should produce a depression in the skin.

(4) If the hernia becomes painful, or if the truss causes distress, report to the clinic for examination.

(5) The hernia must be held back at all times by the truss. You will be able to continue your regular occupation, but if you do any heavy lifting, be certain that the truss is in proper position.

(6) The usual number of injections varies between 8 and 16.

(7) The truss should be worn six months after the last injection. At the end of this period return for check up.

(8) It is also well that you report for examination every two months for about two years after the final check up.

(9) If at any time a recurrence develops, we would appreciate it if you would return for examination or notify us to that effect.

CONCLUSIONS

(1) The ambulant treatment of hernia is a safe and effective method of treating certain types of herniae, if proper technic is used, but there is danger of complications if essentials are not strictly adhered to.

(2) It demands the cooperation of the patient in the proper wearing of the truss.

(3) It brings the mechanical treatment of herniae from the hands of those who know little or nothing of diagnosis, pathology, and anatomy, into the hands of physicians who should know this form of treatment.

(4) Knowledge of the fitting of trusses and the technic of the injection is absolutely essential.

(5) Recurrence of hernia can be very nearly done away with by the combined surgical and injection treatment.

(6) Patients who are incapacitated and have definite surgical contraindications can be so greatly relieved that they may pursue a gainful occupation, and in many cases a cure can be effected. Complications as mentioned have not been substantiated to date by clinical cases.

REFERENCES

[1] Bigelman, Leo: Nonsurgical Treatment of Hernia. Med. Rec., August 21, 1935.

[2] Bratrud, Arthur F.: Ambulant Treatment of Hernia. Lancet, **53**, 673, 1933.

———. The Ambulant Treatment of Hernia. Minnesota Med., July, 1935.

———. The Ambulant Treatment of Hernia. Iowa Med. Jour., August, 1935.

———. The Ambulant Treatment of Hernia. Industrial Med., September, 1935.

[3] Fowler, Samuel W.: Experience with the Injection Treatment of Hernia. Med. Rec., February 20, 1935.

[4] Goldhahn, Richard: Ueber schwere Schädingungen nach Bruchbehandlung mittels Alkoholinjektionen. Klin. Wchnschr., **9**, 1447, 1968, 1969, 1930; **10**, 72, 1931.

[5] Gray, St. Geo. B. Del.: Injection Treatment of Inguinal Hernia. Brit Med. Jour., **2**, 2, 1932.

[6] Hall, James S. K.: Eradication of Hernia by Injections. Experiments and Clinical Investigation with the Method Which Was Originated by Dr. E. P. Mestre of Barcelona. Preliminary Report. Med. Jour. and Rec., **130**, 61, 1929.

[7] Heaton, George: New Treatment of Hernia. Boston Med. and Surg. Jour., **26**, 421, 1843. The Cure of Rupture, Reducible and Irreducible. J. H. Davenport, Editor. Houghton, 1877.

[8] Jacobi, H.: Schwere Schädigung nach Bruchbehandlung mittels Alkoholinjektion. Bemerkungen zu der Arbeit von R. Goldhahan. Klin. Wchnschr., **10**, 71, January 10, 1931.

[9] Jameson, F. Slater, and Cantala, Jr.: Relief of Inguinal Hernia Without Operation. Med. Jour. and Rec., **131**, 87, 1930.

[10] Lannelongue, O. M.: Un tour du monde, Librairie Larousse, 296–297, Paris, 1909.

[11] Mayer, Ignatz: Treatment of Hernia by Subcutaneous Injections. Med. Jour. and Rec., **125**, 528, 1927.

———. Corrective Treatment of Hernia. Med. Jour. and Rec., **135**, 275, 1932.

[12] Mestre, Pina: Las Injectiones Proliferantes Obturados en las hernias. Abstract in J.A.M.A. (edición español), **18**, 186, 1927. (Reported by Mayer.)

[13] McMillan, W. M.: Injection Treatment of Reducible Hernia. J.A.M.A., May 23, 1936.

[14] Quillin, Lawrence, J.: Injection Treatment of Reducible Hernia. Internat. Jour. Med. and Surg., **47**, 394, 1934.

[15] Rice, Carl O.: The Rationale of the Injection Treatment of Hernia. Minnesota Med., September, 1935.

[16] Slobe, Frederick W.: The Injection Treatment of Hernia. Industrial Med., May, 1935.

[17] Velpeau, A.A.L.M.: New Elements of Operative Surgery. Translated by P. S. Townsend, **3**, 554, New York: Wood, 1847.

[18] Velpeau, M.: The Anatomy and Surgical Treatment of Hernia. New York, 272, D. Appleton & Co., 1892.

[19] Warren, J. H.: Hernia, Strangulated and Reducible. Springfield, Illinois, Chas. N. Thomas, 1881.

[20] White, Alfred S., and Harris, Franklin I.: The Injection Treatment of Hernia. Surg., Gynec., and Obstet., August, 1936.

[21] Wolfe, Ralph: Injection Treatment of Hernia. Med. Jour. and Rec., **133**, 242, 1931.

[22] Wollermann: Die Timmermannsche Injektionsbehandlung der Hernien, Aerztl. Rundschau, **39**, 328, 1929.

AN EVALUATION OF THE RESULTS OF THE INJECTION TREATMENT OF INGUINAL HERNIA

A REVIEW OF THE EMPLOYMENT OF THIS METHOD AT THE UNIVERSITY OF MINNESOTA HOSPITAL

Frank S. McKinney, M.D.

Minneapolis, Minn.

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MINN.

Hernia has been defined as a protrusion of some organ or tissue from its natural situation through an accidental or natural opening in the wall of

---

Submitted for publication October 8, 1936.

the cavity in which it is contained, but the mere presence of a perforation or an aperture in the cavity wall, either accidental or natural, through which some organ or tissue may protrude at a later time, is not a hernia. The reduction or elimination of the hernia is effected by the application of a truss. Technically, the hernia is not injected. The treatment is directed to the opening, aperture, canal or rings through which the hernia protrudes. By repeated injections of irritating solutions into the hernial canal, fibrous connective tissue is produced. The hernia is retained by the truss until this tissue reaches its maximum toughness and tensile strength. This treatment is in reality, first, the mechanical or truss treatment of hernia and if this is successful, the injection therapy follows.

General Statistical Analysis.—In the five year period from August 1, 1931, to August 1, 1936, approximately 700 patients have been admitted to the Hernia Clinic of the University of Minnesota Surgical Dispensary. This report concerns 554 patients admitted to the clinic before 1936. Of this number 300 cases had had a sufficient number of injections (at least six) for statistical study. In this group 230 patients returned to the clinic for examination and 70 patients replied by letter or were examined by other physicians. Six months' time had elapsed from the date of the last injection before examination in all cases and in the majority from one to three and one-half years had elapsed. There were 77 patients fitted with a truss who received no injections, 54 patients received three injections or less, 36 patients had irreducible herniae or preferred surgery, 87 patients could not be traced. The age range of patients was from two months to 84 years; average age of this group was 47.5 years (Table I). About 40 per cent of the patients reside in the Twin Cities and have occupations typical of any outpatient dispensary group. The remaining 60 per cent are from the more rural sections of the state. Their predominant occupation is farming.

Table I

	No. of Cases	No. of Injections	Average Age	Youngest	Oldest	Over 50 Years	Over 60 Years
Indirect—Cured	177	16.2	50.9	17 mos.	80 yrs.	34 cases	41 cases
Indirect—Not cured	37	9.6	44.9	5 yrs.	80 yrs.	11 cases	8 cases
Scrotal—Cured	38	16.2	36.5	2 mos.	70 yrs.	5 cases	4 cases
Scrotal—Not cured	5	16.8	52.8	32 yrs.	65 yrs.	1 case	2 cases
Direct—Cured	12	20.1	61.0	46 yrs.	75 yrs.	4 cases	6 cases
Direct—Not cured	3	12.0	67.3	56 yrs.	73 yrs.	1 case	2 cases
Recurrent—Cured	23	15.7	52.8	16 yrs.	84 yrs.	5 cases	9 cases
Recurrent—Not cured	5	19.4	53.4	45 yrs.	61 yrs.	3 cases	1 case

Percentage patients cured—83 per cent.
Percentage patients not cured—17 per cent.

Discussion of Results.—The method used in the treatment of a hernia by injection differs radically from the surgical treatment. Table I shows the number of injections for both cured and noncured cases. Cured cases are those in which we could find no evidence of viscera in the inguinal canal or any abnormal bulging. The gradual elimination of the hernial defect by the injection therapy requires a large number of injections and from the above table some definite conclusions, as to the number of injections required for a given type of hernia, can be drawn. The cured cases in the indirect inguinal group had almost twice as many injections as the failures. In the scrotal type of hernia the failures occurred in the older age group. The cured direct herniae required more injections than the indirect and those listed as failures in the direct group were patients over 50 years of age. It is more difficult to cure herniae with this therapy in aged than in young individuals. In the recurrent group only 28 of our 47 cases (recurrent herniae accounted for 8 per cent of admissions) have been traced. One patient had eight operations on each side; another, three; and nine, two operations. The majority of these cases, if of recent origin, responded quickly, others with large defects in the abdominal wall required a greater number of injections. Sometimes the patients have become discouraged, but a decrease in the size of the hernia occurred in all cases. The injection in the recurrent type of hernia should be made at the internal ring or at the lower angle of the inguinal canal just above the pubic bone. Injections are given every other day until the parts become so swollen that an interval of rest is indicated. When the swelling has subsided and bulging or weakness is still present, injections should be continued.

In the first year of the clinic no scrotal herniae were injected, but, as the clinic grew, an increasing number of patients who had had scrotal herniae for many years presented themselves for treatment. None of these cases was injected, however, until we were satisfied that the truss held the herniae reduced under any physical strain. In many cases a month and in one case three months elapsed before treatment was begun. Older writers on hernia spoke of these scrotal herniae as having lost their right of domicile in the abdomen. Until the viscus resumes its normal habitat in the abdomen it is useless to start injections. The presence of a large sac (which in this form of therapy is not removed) may mean a slight recurrence of the hernia in six months or a year. Our patients are instructed to present themselves every three or four months up to two years after the first series of injections. In practically every case where a recurrence developed, only a small number of injections, usually three or four, were necessary to close this defect. Whether our failures are recurrent herniae or insufficiently injected cases is sometimes difficult to answer. Many of our early cases recurred, but they had had a minimum number of injections. The patients insisted on more injections because the recurrence was smaller than the original hernia. Usually a case where the hernia recurs in a short time after the removal of the truss can be classified as one insufficiently injected, but, after a lapse of several months, as a recurrence. Four cases required more than 40 injections; one case required 52 injections spread over a two year period. The prolonged treatment was due to the failure of the first truss to completely retain the hernia. A large stock of trusses is kept on hand because the patients are fitted in the clinic. For a while the patients were allowed to retain the truss they were wearing, but many of these cases did not respond well to treatment and time can be saved if the patient is fitted with a new spring truss. A correct pad for each patient is just as important as the truss itself. The obese, overweight person required a larger and thicker pad than the average individual. The oversized truss has given us better results than the one fitted exactly to the patient's measurements.

Results with Reference to Various Age Groups.—A group of 15 children under 13 years of age were injected; only two cases (girls 7 and 11) reported by letter that their herniae were not cured after six injections. The other 13 cases were examined at the clinic. In this group were two infants (2 months and 17 months respectively). Both of these cases had had scrotal herniae since birth and examination after two years revealed a complete closure of the inguinal canal. The treatment of infants and children by injection is disagreeable due to the psychic element. The majority of our failures were in patients past 50 years of age. The obese, overweight individual is a poor subject for injection therapy. Herniae present for a great many years, with resulting damage to the abdominal wall, do not respond so quickly to this form of therapy as those of recent origin.

Treatment of Hernia in Patients Where Surgery Is Contraindicated.—Two hospital cases ill with tuberculosis and enterocolitis respectively, had scrotal herniae. The descent of the herniae by coughing and bowel movements caused them intense pain. Injections into the inguinal canal blocked the descent of the herniae.

Treatment of Miscellaneous Groups (three epigastric, seven umbilical, and five femoral herniae).—The epigastric herniae can be treated if the defect is small. In a femoral hernia the pad of the truss rests on the thigh and in this position is easily displaced by muscular movement. Success of treatment depends upon complete reduction of the hernia by the truss. Injection should be made cautiously due to the close proximity of the femoral canal to the femoral vessels. The treatment of small umbilical herniae has been satisfactory.

Complications.—The most frequent complication is the swelling of the spermatic cord. Five patients from this group of 700 patients were admitted to the University Hospital for other reasons, however.

(1) Patient, age 76, had a large scrotal hernia which had been present for 30 years. The hernia strangulated following the fitting of a truss. He had no injection. Operation. Recovery.

(2) Patient developed a severe pain in back and side following injection. A slough (size of a dollar) opposite umbilicus from injection of deep epigastric artery. Slough healed in three weeks.

(3) Patient had symptoms of local peritonitis (nausea and vomiting) following injection for recurrent hernia. Operation. Small area of local peritonitis found. Repair of hernia. No drainage. Uneventful recovery.

(4) Patient with abscess following injection for a recurrent hernia after appendicectomy. Drained three weeks. Recovered.

(5) Patient with large scrotal hernia. Injection made into the sac of the hernia. Large swelling of scrotum. Patient in hospital five days. Complete recovery.

Two other patients seen outside of the University Outpatient Clinic in consultation presented the appended complications.

(1) A patient injected for hernia developed, three days later, an embolus or thrombus in the anterior tibial artery on the same side He lost one toe, but collateral circulation had been reestablished. The patient had previously complained of cramps in the legs and suffered from generalized arteriosclerosis.

(2) Patient developed an abscess following the accidental injection of one cubic centimeter of Proliferol into a blood vessel of the spermatic cord. An abscess was about two weeks in developing. Drainage. Uneventful recovery.

There has been no mortality either directly or indirectly in this group of 700 cases as a result of injection therapy. A patient entered the University Hospital with peritonitis following injection for a hernia by another physician. This patient died in the hospital. Autopsy revealed a perforation of the ileum. The absence or presence of varicocele, spermatocele, hydrocele, swelling of epididymis or atrophy of the testicle should be noted before treatment is begun. Distinct atrophy of the testicle was found in 20 of the 300 cases. Mumps and trauma were given as likely etiologic factors. Two cases were congenital. Atrophy of the testicle has not occurred as a result of injections for hernia. It is almost a truism, found in every text-book on surgery, that the truss is the most important cause of strangulated hernia and we expected this as a frequent complication. Only two cases of strangulation have occurred, one listed above (1) and the other a woman whose hernia strangulated after 15 injections.

Evaluation of the Injection Method

Disadvantages.—(1) The long period of time required to obtain a wholly satisfactory result.

(2) Uncertainty as to the number of injections each individual case requires.

(3) Inability of some patients to keep the hernia reduced by the truss (a scrotal hernia in a young farmer did not respond to injection treatment. It was the patient's habit to remove his truss the second or third day after injections because of soreness. After one treatment he lifted 150-pound cakes of ice all day without his truss).

(4) Sickness, accidents, lack of funds for transportation and change of residence and occupation frequently cause either prolonged or inadequate treatment.

(5) Too often the patient makes his own diagnosis as to the cure of his hernia (the swelling produced by the injection blocks the hernia. He then believes a cure has been obtained. When the edema and swelling subside he may find his hernia recurring. Actually his hernia was not cured and what we observe is a natural process, the absorption of the products of inflammation. Frequent examinations are necessary before we can be sure sufficient injections have been given).

ADVANTAGES.—(1) Patient is able to continue his regular occupation.

(2) No serious complications have resulted from the injection treatment.

(3) Patients suffering from constitutional diseases, where surgery is contraindicated, can receive treatment.

(4) In the recurrent herniae following operation, if the defect is not too large, this method offers the patient a way out of his difficulty if he does not wish another operation.

(5) Applicability to patients of advanced age (while difficulties have been experienced in closing herniae in the older age group that have been present many years, some excellent results have been obtained in aged patients).

CONCLUSIONS

The merits of hernioplasty versus the injection treatment is a question naturally asked. In some respects the problem is identical with the question of medical treatment versus surgery in the treatment of peptic ulcer. The medical treatment may require several months, the surgical often one operation. The impossibility of standardizing this method with respect to the number of injections and length of time treatment is required and also its ambulatory nature (success depending on the patient's cooperation) have been factors in many poor results. *Too much emphasis has been placed on the injected solution and not enough on a proper fitting of the truss.* The injection therapy has a place in the cure of hernia and instead of condemning it as quackery, surgeons should add it to their armamentarium in the treatment of hernia. The small hernia in the young individual offers the *ideal* case for treatment by this method.

THE INJECTION TREATMENT OF HERNIA

AN EVALUATION OF THE TECHNIC AND RESULTS

CARL O. RICE, M.D.
MINNEAPOLIS, MINN.

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF MINNESOTA, AND THE MINNEAPOLIS GENERAL HOSPITAL
MINNEAPOLIS, MINN.

THE technic which is employed at the Minneapolis General Hospital for the cure of hernia, by the injection method, carries out the same principles as those which are employed in the surgical treatment of this condition, *i.e.*,

---

Submitted for publication October 8, 1936.

the closure of the defect through which the hernia passes and the occlusion of the hernial sac.

Whether or not these principles are accomplished by one method or another should make no essential difference as long as the risk of doing it is not increased and the end-results are satisfactory. Likewise the solution which is employed to cause the irritation, and thereby produce fibrous tissue hyperplasia, is of secondary importance as long as the solution does not produce too extensive damage to the tissues. There are some side-effects produced from the injection of some of the solutions, which have been employed for this purpose, which, though they may not be harmful, seem undesirable. Among these are excessive exudative reaction in the tissues following injection, pain produced from the injection and the danger of systemic reaction from an inadvertent intraperitoneal or intravenous injection.

There are a number of solutions which have been recommended for the injection treatment of hernia. These solutions are essentially of two different kinds: Those containing an acid in alcoholic solution or caustic salts (the principle ones of which are tannic acid, phenol and zinc sulphate) and those consisting of a mild soap solution. Most all of the solutions produce the desired irritation and the development of fibrous tissue but some of these present undesirable features because of their excessive irritating qualities, pain produced from their injection or danger from systemic reaction if inadvertently injected into the blood stream or peritoneal cavity. This is particularly true of the acid-alcohol solutions. It appears, from the evidence obtained at the Hernia Clinic of the Minneapolis General Hospital, that the mild soap solution which we have employed possesses advantages which have not been obtained from the use of the acid-alcohol mixtures.

Factors in Determining the Selection of Cases.—The selection of suitable cases for the injection is a large factor in the determination of the end-results. It is not presumed that every hernia can be cured by the injection method. On the other hand, an unwise selection of cases will materially decrease the percentage of cures and thereby detract from the true value of the method. Experience has taught the value of judicious selection. In order to be suitable for the injection treatment the hernia must be first reducible and capable of being retained with a properly fitting truss.

As the external ring is the only measurable criterion by which the suitable case can be selected, an effort has been made to determine, from this physical finding, those cases which are satisfactory subjects. If the external ring measures more than 3 cm. in diameter, it has been found that a cure is difficult to obtain. For that reason we have arbitrarily chosen to exclude from the injection treatment, individuals whose external ring is larger than 3 cm. in diameter.

Excessive obesity is also a contraindication for the injection treatment. It may be difficult to define at what stage a person may be considered excessively obese but for our purposes if the obesity is sufficient to make examination and identification of the inguinal anatomy difficult it is then sufficient to make a cure by the injection method unsatisfactory.

Individuals who are required to strain at stool or while urinating; those with a chronic uncontrollable cough or any other condition which will produce abnormally increased intra-abdominal pressure are not accepted for the treatment until these factors have been controlled.

Age is not a factor. The young as well as the aged can be satisfactorily treated and cured. Syphilis, diabetes, hemophilia and a number of other diseases have been considered contraindications but these do not constitute absolute contraindications and may be left to the judgment of the physician.

Technic.—The accompanying drawings illustrate clearly the mechanics of depositing the solution in the proper position. The details of the technic have been more fully dealt with by Dr. Bratrud.

DIRECT INGUINAL HERNIA.—In cases of direct inguinal hernia the plane of the weakened transversalis fascia, overlying the lower half of Hesselbach's triangle, is infiltrated with the irritating solution by placing the injections successively, at two or three day intervals, in the areas indicated by the numerals 1 to 10 (Fig. 1). This accomplishes the purpose of closing the defect through which a direct hernia passes, just as is done at the surgical operation when suturing the conjoined tendon to Poupart's ligament, under the cord. In this type of hernia the sac drops back into the peritoneal cavity and is, presumably, eventually contracted and obliterated by the scar tissue which is formed above it in the plane of the transversalis fascia.

Twelve injections have been found to be the average number required for the direct inguinal hernia.

INDIRECT INGUINAL HERNIA.—In cases of indirect inguinal hernia the internal ring is first constricted by injections placed circumferentially around the cord at the point where it makes its exit from the abdominal cavity, as indicated in Fig. 2 by numerals 1, 2, and 3. This constriction of the internal ring accomplishes the same principle as is accomplished at the surgical operation when the internal ring is made narrower with the aid of a Coley's stitch. Subsequent injections are placed circumferentially around the cord, in the inguinal canal, as indicated in Fig. 2 by the numerals 4 to 10. These tend to constrict the inguinal canal just as is effected at the surgical operation when the fascia of the external oblique is sutured over the cord. A few additional injections are placed in the plane of the transversalis fascia just as is done for the direct inguinal hernia (Fig. 1). These latter strengthen the floor of the inguinal canal and are comparable to suturing, at operation, the conjoined tendon or one of the leaves of the external oblique fascia to Poupart's ligament, under the cord. It is important to place a few of these latter injections at the lower angle of Hesselbach's triangle, near the pubic tubercle, in order to reinforce this area, as is so often emphasized at the surgical operation when the young surgeon is taught to catch the first stitch directly into the pubic tubercle and fasten it to the apposing end of the ilio-inguinal ligament.

Those injections which are placed superficial to the cord but under the fascia of the external oblique muscle (this being the most superficial position of the hernial sac) cause the inflammatory reaction to extend into the hernial sac and thereby occlude it as its two apposing surfaces become adherent to one another with newly formed fibrous tissue. This contention has been positively demonstrated in two cases which were pronounced cured of their hernia and who were subsequently explored during the performance of an incidental appendicectomy through a low transverse-oblique incision.[9] In addition, proof has been afforded from the observation of several cases in which an hydrocele corresponded in position to the previous location of the hernial sac. The hydrocele fluid could not be forced back into the peritoneal cavity, indicating that the neck of the herinal sac had been occluded. These hydroceles have all been aspirated (the diagnosis thereby confirmed) and a small quantity of the irritating solution injected into their lumen, eventually resulting in their complete and permanent eradication.

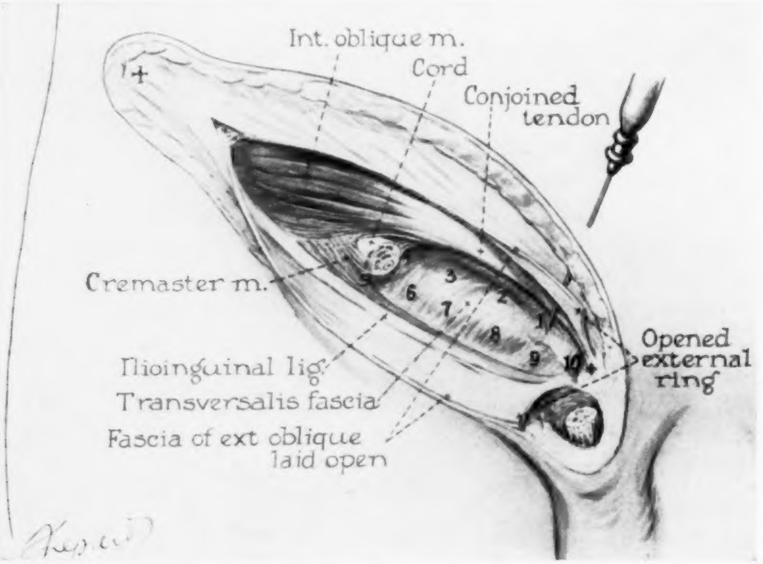

Fig. 1.—Method of injecting a direct inguinal hernia. The injections are made at the sites indicated by the numerals 1 to 10. These are in the plane of the transversalis fascia, lying below the level of the spermatic cord.

In both the direct and indirect inguinal hernia the external ring is made smaller by injections placed around the margin of the external ring, in the plane of the fascia of the external oblique (Fig. 3).

The average number of injections for the cure of indirect inguinal hernia has been found to be 10. Some cases have been cured with fewer injections, whereas others have required as many as 20 to 30 injections. These latter are, no doubt, some of the cases which did not receive the injections in the proper position or were patients in whom it would have been better to have recommended surgical operation.

General Considerations and Precautions.—The approach to the inguinal region is made from above downward, with the needle held at an angle of 40° with the skin of the abdomen. This approach, we feel, avoids the danger of entering the peritoneal cavity, as at this location the peritoneal cavity slopes away from the surface plane of the abdominal wall. There are certain definite symptoms produced if the needle encroaches upon the peritoneum or the spermatic cord. If the peritoneum is punctured, or touched with the needle point, the patient experiences pain throughout the lower part of the abdomen and reflexly tenses the lower abdominal muscles with a quick sudden jerk. If the injection is continued and the solution deposited into the peritoneum the patient will experience a shock-like reaction, with cold sweat, slow pulse, pain and rigidity of the lower abdominal muscles. These symptoms will subside within 20 or 30 minutes and leave no residual effects unless the solution has entered the peritoneal cavity, in which event the symptoms will persist for two or three days, eventually subsiding without harmful effects. This complication requires observation but no surgical intervention unless the bowel appears to have been injured. If the spermatic cord has been punctured the patient will experience pain which radiates into the penis or testicle. If the solution is injected into the cord an induration of the cord will result. If the tannic acid-alcohol solution is injected intravenously, an accident which may occur inadvertently, the patient will experience a shock-like reaction which may rightfully give cause for a great deal of apprehension.

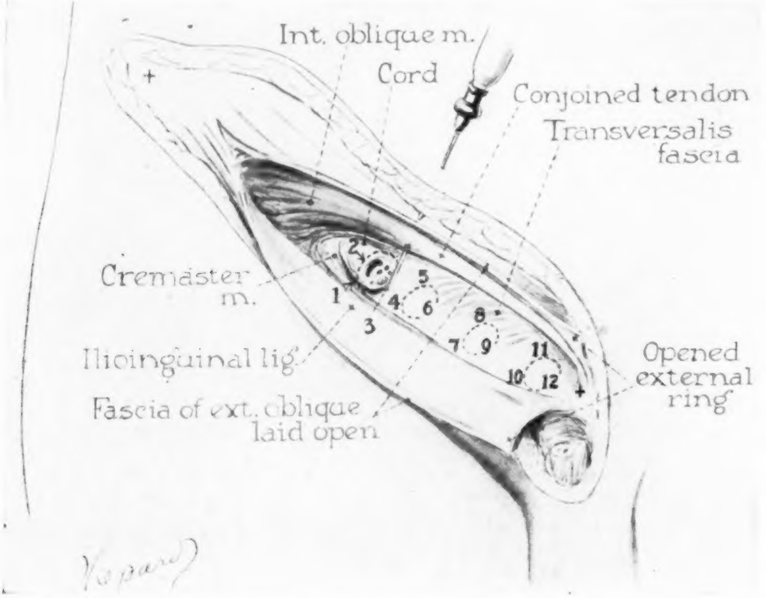

FIG. 2.—Method of injecting an indirect inguinal hernia. The injections are made circumferentially around the cord, as indicated by the numerals 1 to 12. The first three injections are made around the internal ring. Subsequent injections are placed around the spermatic cord. A few additional injections are placed in the plane of the transversalis fascia as indicated in Fig. 1, particularly at the sites indicated by numerals 1, 2, 8, 9, and 10. (These drawings are a copy of those which have been previously published in the Southern Surgeon.[9])

The intravenous injection of the soap solution gives the patient the taste of soap and a tingling sensation of the body from which they recovered within a few minutes.

The use of a local anesthetic, preliminary to the injection, has not been considered advisable as it may disguise the signs, as mentioned above, which would otherwise help to avoid a misplaced injection. In using the soap solution the pain from its injection is so mild that it has never been considered necessary to use a local anesthetic. The tannic acid-alcohol or the zinc sulphate solutions produce so much pain from their injection that it is often difficult to obtain a continued cooperation of the patient unless a local anesthetic is injected a few minutes before.

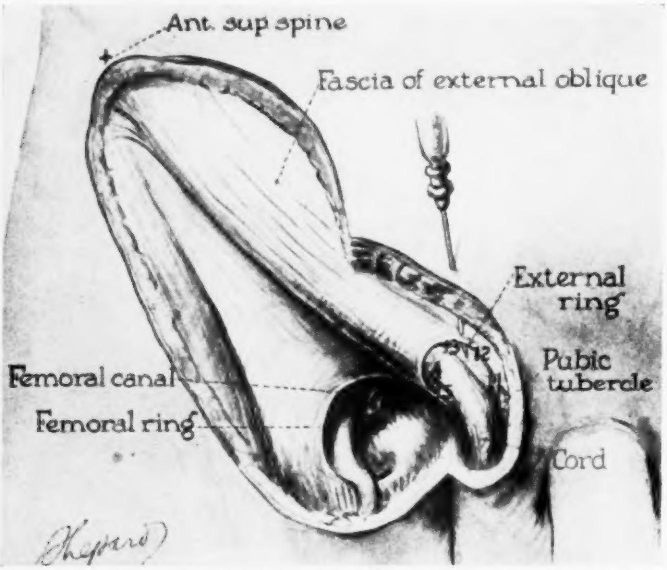

FIG. 3.—Method of injecting the external ring in both direct and indirect inguinal herniae. Note how the needle passes first through the fascia of the external oblique at the margin of the external ring. This is done so as to get the solution below the external spermatic fascia which passes from the external ring to the spermatic cord at this point.

END-RESULTS.—It is of interest to mention the statistics of Wollermann[11] who made a comparison of the injection method with those of the surgical operation (Table I).

TABLE I

	Injection Method	Operative Method
Total number of cases treated	2,949	1,140
Exaggerated reaction and swelling without suppuration	33	130
Prolonged suppuration (deep abscesses, fecal fistula, *etc.*)	20 (.7%)	23
Testicular atrophy	2 (.07%)	5
Deaths	1 (.04%)	5

The average incidence of cures, as compiled from the figures cited in the literature by Kretzschmar, Mayer,[8] Campos and Subirachs,[4] Jameson, Wolfe,[10] Wyss,[12] Gray,[7] Wollermann,[11] and Bratrud, totaling 6,550 cases, was 92.6 per cent. The results which we have obtained by questionnaire from 23 doctors revealed 2,216 cases treated and controlled. Eighty-five per cent of these were cured.

A review of the cases at the Minneapolis General Hospital revealed 804 individuals with 1,025 herniae. In 213 of these patients treatment was advised but not given because the patients did not return; 115 patients were referred directly for surgical operation since it was felt that in these patients the hernia would not respond favorably to the injection treatment; 97 of the patients have not received sufficient treatment to be pronounced cured. Some of these have not returned for more treatments and may be cured but have not been included in the known results because we have not been able to obtain a final check up. Cures have been obtained in 379 patients with 445 herniae. Eleven have failed to respond to the treatments. The cure of these cases has been determined by personal follow up observation. No patient has been pronounced cured until the check up examination has revealed "no impulse" for a period of six months after the last treatment and until the patient has been without his truss for at least four months. No deaths have occurred in any of the treated cases.

If only the controlled cases are calculated, 97.6 per cent cures are obtained. Comparing these figures with those which are reported from the surgical treatment, in which statistics ranging from 3 to 30 per cent of recurrences are recorded, it would seem that the injection method offers some advantages. Gibson and Felter,[6] reviewing 1,618 surgical cases, found recurrences in 2.9 per cent. Cattell and Anderson[5] found 6.7 per cent recurrences with unilateral hernia and 18.1 per cent with bilateral herniae. Block[2] made a study of a large series of European cases and found recurrences in 3.5 per cent of the herniae treated by surgery. Andrews and Bissell,[1] from a review of cases treated at the Johns Hopkins Hospital, the Massachusetts General Hospital and the Presbyterian Hospital in New York found that recurrences ranged from 4.1 to 32 per cent with an average of 20 per cent.

Complications and Sequelae.—Seventy-eight of the 445 cured herniae reported in this paper developed complications, or sequelae, at one time or another during the course of treatment. These complications were as follows: Induration of the cord, 44 cases; superficial ulceration of the skin, as a result of the truss irritation, eight cases; severe pain, suggesting peritoneal irritation, ten cases; chemical peritonitis, two cases; hydrocele of the cord, seven cases; local abscess, two cases; dermatitis, one case. The first three of these complications are of no prognostic significance. The induration of the cord might be compared to the induration of the wound, following surgery. It is rare that anyone ever mentions this as a surgical complication. It adds no difficulties to the healing and does not endanger the life or health of the individual. In fact it probably indicates that the hernial sac is being obliterated by fibrous tissue formation between its two apposing surfaces. There is histologic evidence to substantiate this contention, as has been shown in a previous publication.[9] Superficial ulceration of the skin, from the truss irritation, would occur whether or not the injections were given. Pain from the injection, too close to the peritoneum, is comparable to the pain which is experienced when the peritoneum is pulled upon at the time of operation if local anesthesia is being used. Therefore, if these three sequelae are excluded from the list of complications so as to make a series which can be compared with the surgical complications, we find the incidence of 4 per cent.

Gibson and Felter reviewed 1,618 surgical operations for hernia. They found complicating factors in 368 of these. Some of these untoward results were evidently not the direct result of the surgical operation. Among these were pneumonia, 34 cases; bronchitis, three cases; cough, 30 cases; infarcts, eight cases; pulmonary tuberculosis, five cases; epididymitis, two cases; varicocele, 23 cases; hydrocele, 74 cases; laryngitis, empyema and influenza, each one case. Among the cases which appear to have followed as a direct result of the surgical operation there were 70 cases of wound infection; 59 hematomata; 21 orchitis; two accidental incisions of the bladder, and one each of accidental cutting of the spermatic cord, a large artery, and the sigmoid colon. If these latter complications are included among the complicating cases so as to make it comparable to our injected cases it is found that the incidence of complications from the operation is 9.7 per cent. This figure represents a little more than twice as great an incidence of complications as that which we have observed from the injection treatment.

CONCLUSIONS

With these briefly stated facts, comparing the surgical results and complications with those from the injection method, it appears that the injection method offers a procedure, to the medical profession, which should have a very decided value in the treatment of carefully selected cases of hernia. The technic is not difficult and can be acquired by anyone who wishes to take a little time to study the method. It must be carefully performed, however, in order to obtain the most satisfactory results.

REFERENCES

[1] Andrews, E., and Bissell, A. D.: Direct Hernia. A Record of Surgical Failures. Surg., Gynec., and Obstet., **58**, 753–761, 1934.

[2] Block, W.: Bericht über eine Sammlung von 20,199 Leistenbruchoperationen. (Rezidive) Arch. f. klin. Chir., **175**, 607–624, 1933.

[3] Bratrud, A. F.: The Ambulant Treatment of Hernia. Minn. Med., **18**, 441–451, 1935.

[4] Campos and Subirachs: The Treatment of Hernia by the Fibrogenous Method. Información Med., **6**, 155, 185, 1929.

[5] Cattell, R. B., and Anderson, C.: End Results in the Operative Treatment of Inguinal Hernia: A Report of 150 Cases at the Lahey Clinic. New England Jour. Med., **205**, 430–432, 1931.

[6] Gibson, Chas. L., and Felter, Robert, K.: End Results of Inguinal Hernia Operation. ANNALS OF SURGERY, **92**, 744–753, 1930.

[7] Gray, St. G. B. de L.: Injection Treatment of Inguinal Hernia. Brit. Med. Jour., **2,** 12–14, 1932.

[8] Mayer, Ignatz: The Treatment of Hernia by Subcutaneous Injection. Med. Jour. and Rec., **125,** 528, 596, 672, 1927; **128,** 415, 1928; **131,** 90, 1930.

[9] Rice, Carl O., and Larson, L. M.: Technique for the Injection Treatment of Hernia. Southern Surgeon **5,** 227–233, 1936.

———. The Fate of the Hernial Sac in Hernia Treated by the Injection Method. Western Jour. Surg., **44,** 428–429, 1926.

Rice, Carl O., and Mattson, Hamlin: The Histologic Changes in the Tissues of Man and Animal Following the Injection of Irritating Solutions Intended for the Cure of Hernia. Illinois State Med. Jour., September, 1936.

Rice, Carl O.: The Rationale of the Injection Treatment of Hernia. Minn. Med., **18,** 623–626, 1935.

[10] Wolfe, Ralph: Injection Treatment of Inguinal Hernia. Med. Jour. and Rec., **133,** 243–246, 1931.

[11] Wollermann: Die Timmermannsche Injektionsmethode in den letzten 25 Jahren. Aerzt. Rundschau, **39,** 283–284, 1929.

[12] Wyss, Franz: Die Behandlung der Hernien mit Alkoholinjectionen. Schweiz. med. Wchnschr., **59,** 85–89, 1929.

STERILITY FOLLOWING THE INJECTION TREATMENT OF HERNIA

A DETERMINATION OF ITS INCIDENCE

CHARLES E. REA, M.D.
MINNEAPOLIS, MINN.
FROM THE DEPARTMENT OF SURGERY OF THE UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MINN.

STERILITY has been impugned as a complication of the injection treatment of inguinal hernia in the male. This suggestion occasioned the writer to investigate the potential sterility of patients with bilateral inguinal herniae who had been subjected to this type of treatment. No one has apparently deemed it necessary to inquire into the question of possible sterility following the operative repair of hernia. That the possibility for such an occurrence exists is evident in that in large series of operations, undertaken for the cure of indirect inguinal hernia, postoperative swelling of the testis appears as a complication in about 6 per cent of cases; such postoperative testicular swelling leaves the patient with an indurated, enlarged, or atrophic testis (Taylor,[8] Cattell and Anderson[1]). The occasional swelling of the spermatic cord accompanying the injection treatment of hernia prompts this investigation.

The problem of impotence is not to be confused with that of sterility. Impotence is a disturbance of function; sterility a failure of reproduction. A man may be impotent but fertile, and *vice versa.* Impotence presents varying degrees of disturbance of normal coitus, from premature ejaculation to total loss of erection. The causes of impotence may be primary or functional (loss of potency from psychic inhibitions) or secondary to organic pathology

---

Submitted for publication October 8, 1936.

(loss of potency due to a lesion in the genitalia, the endocrines or nervous system (Hinman[2]). Ripe spermatogenesis, free seminal transmission and successful coitus are the prerequisites for fertility in the male.

Theoretically it is conceivable that injecting a sclerosing solution around the inguinal canal might cause stricture or obstruction of the vas deferens or injury of the nerve or blood supply to the cord or testis. Actually, however, Rice,[5] in a series of 30 cases of hernia that had received injections but who were later subjected to operation, observed no difference in the cord as compared to normal. A few had as many as six to eight injections, the rest less than two. If there is a mechanical factor involved, one would think that sterility more than impotency would be affected. Rubin[6] thinks that impotency is largely psychic, and that in only 5 to 10 per cent of cases is there a mechanical defect.

To date, 75 patients with unilateral inguinal hernia treated within the last two years at the University of Minnesota Outpatient Clinic have been questioned individually as to their potency. They were questioned as to libido, frequency of erection and intercourse, *etc.*, before and after hernial injection, trying to control other factors (age, neurosis, prostatitis, *etc.*). Seventy-four patients stated that they had noticed no difference. One patient, a healthy male, age 43, stated that his libido was definitely decreased for three months following his injections. The sterility factor was not investigated in the unilateral cases.

More suitable for this type of study is the patient who has received injections for bilateral inguinal herniae. Twenty-six such cases were investigated. All were males, and the ages ranged from 20 to 72. These patients had received from four to 28 injections. No case had been followed for more than three years. Of the 26, two claimed there was a decrease in libido following injections. One, a neurotic male, age 52, who had been treated for bilateral indirect inguinal herniae, chronic prostatitis, varicose veins and hemorrhoids, stated that he began to have painful erections after three years of injection treatments, causing him to avoid intercourse. The other patient, a male, age 20, who admitted extramarital intercourse and who might be diagnosed as having a mild case of satyriasis, complained that for five months after 13 bilateral injections he had less libido and less frequent erections.

To study the possible sterility in these treated cases of bilateral inguinal herniae, ejaculation tests were performed. If this was unsuccessful, prostatic smears were examined for spermatozoa. In health, a normal male is capable of producing and ejaculating 3 to 5 cc. of semen containing 300 to 400 millions of spermatozoa (Rubin). Following this criterion, in 15 cases in which ejaculation tests were performed after treatment, all were normal. In two cases, ejaculation tests were obtained before and after treatment; one of the patients had had an operative repair on one side. In eight patients from whom prostatic smears were obtained, no spermatozoa were found. Three of these cases had a chronic prostatitis. The unreliability of prostatic smears as a test for fertility has been noted by Wangensteen.[9]

SUMMARY.—In this study the incidence of sterility and impotency as a complication following the injection treatment of hernia is not impressive. In a series of 26 bilateral inguinal herniae, followed up to three years, ejaculation tests were performed in 15, all of which showed normal fertility. Two patients, both of whom showed abnormal mental traits, complained of less libido three months and five years, respectively, after hernial injections. In a series of 75 unilateral inguinal herniae, followed up to two years, only one complained of less libido after a course of sclerosing injections. As to impotency following injections, the type of patient is probably the most important factor.

CONCLUSIONS

Twenty-six patients who had received injections for the cure of bilateral inguinal herniae submitted to semen examinations to test their potential fertility. In all, spermatozoa counts within the normal range were obtained. Sterility would not therefore appear to be a complication of the injection treatment of hernia. Fear of such an occurrence should not deter employment of this method in the treatment of selected cases of inguinal hernia.

REFERENCES

[1] Cattell, R. B., and Anderson, C.: End-Results in Operative Treatment of Inguinal Hernia. New England Jour. Med., **205**, 430, 1931.

[2] Hinman, F.: Principles and Practice of Urology, **831**, W. B. Saunders, 1935.

[3] McMillan, W. M., and Cunningham, D. R.: The Injection Treatment of Hernia. J.A.M.A., **106**, 1791, May 23, 1936.

[4] Nelson, A. N.: Personal Communication. Dept. of Pathology, Univ. of Minnesota.

[5] Rice, C. O.: The Rationale of the Injection Treatment of Hernia. Minn. Med., **18**, 623, 1935.

[6] Rubin, I. C.: Sterility. Lewis System Surg.

[7] Strauss, O. A.: Injection Method for Hernia (Correspondence). J.A.M.A., **105**, 1702, November 23, 1935.

[8] Taylor, A. S.: The Results of Operation for Inguinal Hernia. Arch. Surg., **1**, 382, 1920.

[9] Wangensteen, O. H.: The Undescended Testis. Its Fate after Satisfactory Scrotal Anchorage. ANNALS OF SURGERY, **102**, 875, 1935.

THE VALUE OF PARTIAL PANCREATECTOMY IN CONVULSIVE STATES ASSOCIATED WITH HYPOGLYCEMIA

John M. McCaughan, M.D., Ph.D., and G. Owen Broun, M.D.
St. Louis, Mo.

FROM THE DEPARTMENTS OF SURGERY AND INTERNAL MEDICINE, ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS, MO.

The successful treatment of disorders of the glands of internal secretion by operative methods is one of the great triumphs of modern surgery. The earliest important advance in this field was made in the treatment of goiter where the removal of a sufficient amount of overfunctioning thyroid tissue was followed in most instances by the relief of symptoms. As clinical experience increased, dysfunction in other endocrine organs was recognized and in time definite glandular syndromes were established for which relief by surgical measures was sought. Important among these were diseases of the gonads, the parathyroids, the pituitary gland, the adrenals and the pancreas.

The surgical treatment of hyperinsulinism may be said to be in its pioneer stage; nevertheless, the history of its development even thus far is of considerable interest. Seale Harris, in 1923, is credited with having hypothecated the clinical concept of hyperinsulinism. In 1924,[4] he was able to collect several cases with nervous symptoms and low blood sugar readings. Parker and Finley,[7] in the same year, also published reports on ten cases with hypoglycemic manifestations which could be reasonably explained on the basis of excessive insulin production within the body. It was not, however, until Wilder, in 1927,[11] published the result of an operation performed upon a patient by W. J. Mayo, that the hypothesis of Harris received verification. The patient in this instance had a malignant tumor of the pancreas with metastases to the regional lymph nodes and the liver. The most interesting thing about this tumor, however, was that it was composed of cells resembling the cells of the Islands of Langerhans. Following Wilder's article, sporadic reports of similar cases began to appear in the literature. In the vast majority, the symptoms were far too mild to demand radical measures for relief but in a recent review of the subject by Whipple[10] a total of 57 cases with tumors of the pancreas was collected. Of these 57 cases, however, only 27 actually had hypoglycemic symptoms. Thirty of the cases were without recorded hypoglycemia. Of these 27 cases of tumor with hypoglycemic symptoms, there were 18 in which the tumor was found at operation and nine in which the tumor was found at necropsy. In addition there were 18 other cases of hypoglycemia in which no tumors were found; 15 of these by surgical exploration and three by necropsy. Of these 15 operative cases without adenoma, the pathologists reported a normal pancreas in ten, pancreatitis in

---

Submitted for publication September 8, 1936.

three, hypoplasia in one, and hypertrophy in one. In the three cases coming to necropsy all were said to exhibit hypertrophy of islet tissue. It must be admitted, however, that it is an exceedingly difficult task, for pathologists to recognize significant departures from the normal number and volume of islets in histologic sections by ordinary methods. Bensley[1] and later Thompson[9] have made accurate enumerations of the Islands of Langerhans in man and laboratory animals and the methods employed by these investigators appear far too complicated and laborious for routine pathologic diagnoses.

Unfortunately, it will be noted after analysis of the foregoing figures of Whipple that in almost two-thirds of the cases with hypoglycemia there was no demonstrable tumor present so that the operator had to assume: (1) That the pancreas was normal and the hypoglycemia was perhaps of extrapancreatic origin; (2) that there was a more or less diffuse hyperfunction or hyperplasia of islet tissue or (3) the existence of a small adenoma hidden deep within the parenchyma of the gland, not evident on ordinary inspection and palpation. However the case, the majority of surgeons, when faced with this situation, have, after thorough exploration of the abdomen has failed to reveal any other pathology, attempted the ablation of varying amounts of the pancreas; probably on the assumption that a hidden tumor might luckily be brought to light or that extirpation of sufficient pancreas might so reduce the total amount of insulinogenic tissue that the symptoms of hypoglycemia, whatever the cause, might be completely relieved or at least brought under partial control.

The results of surgical treatment have been truly astonishing in patients with definite tumor tissue but in the patients without pancreatic tumors the results have been much less satisfactory. The experimental investigations of Houssay and his coworkers[5] on the importance of the pituitary gland in relation to carbohydrate metabolism in laboratory animals may eventually have a significant bearing on the judgment and decision of the surgeon when at operation he finds no definite pancreatic, adrenal, hepatic or gonadal pathology. At all events, their studies on the correlation between the anterior hypophysis (diabetogenic hormone) and the pancreas are most interesting and very possibly explain the hyperinsulin syndrome in patients without pancreatic adenomata. It is most unfortunate that at the present time there is no satisfactory way of distinguishing the several possible varieties of hypoglycemia from one another. For example, it would be most desirable to differentiate the types due to disturbance in other viscera such as the liver, adrenals, gonads and pituitary gland from those originating primarily in the pancreas. Berry[2] has made the interesting suggestion that in functional hyperinsulinism as opposed to adenoma, increasing doses of glucose are necessary in preparing blood sugar cures, which tend to be lower with larger doses. Furthermore, he believes that starvation causes a rise in blood sugar in functional hyperinsulinism.

Appended is a report of six cases exhibiting convulsions and hypoglycemic sugar tolerance curves which were studied in association with Dr.

Broun of the Medical Service at Firmin Desloge Hospital. The operative technic has been described in a previous publication.[5]

Case 1.—C. Z., white male, single, age 20, was admitted to the Firmin Desloge Hospital October 22, 1934, complaining of convulsions occurring periodically during the past three years. These seizures occurred usually at night and were characterized by complete unconsciousness and generalized convulsions. The patient had a voracious appetite and was particularly fond of sweets. There were no previous diseases of importance and the family history was entirely negative. The neurologic and general physical examinations were essentially negative. Blood pressure 115/77. Roentgenologic examination of the chest revealed a chronic bronchitis and a moderate degree of cardiac enlargement.

Laboratory Data.—Urine negative. Blood: Leukocytes, 6,050; erythrocytes, 4,560,000; hemoglobin, 89 per cent. Blood Wassermann, negative. The sugar tolerance curves, November 23, 1933, and October 5, 1934, were low (Chart 1). The maximum blood sugar was 104 mg. per 100 cc. and the minimum blood sugar was 52 mg. per 100 cc. of blood. A diagnosis of possible hyperinsulinism was made and on October 27, 1934, a subtotal pancreatectomy was performed, 8 Gm. of tissue being removed from the tail of the pancreas.

Pathologic Examination.—The pancreas was sectioned at intervals of a few micra each, without finding any adenoma. The islet tissue was markedly increased due to an increase in number rather than in size. There was one small area of fat necrosis and pancreatic degeneration.

After operation the patient continued to have convulsions which for a time occurred with about the same frequency but with greater severity than prior to operation. Since July of 1935, however, the attacks have been somewhat milder and not nearly so frequent. Chart 2 shows chronologically, the frequency of major seizures before and after operation. Sugar tolerance tests were performed December 4, 1934, and March 4, 1935. The former was in the hypoglycemic zone but the latter was within normal limits.

Case 2.—E. T., male, age 17, was admitted to the hospital November 9, 1934, complaining of "fits." His illness had begun four years ago with a seizure characterized by unconsciousness and generalized convulsions. These attacks frequently occurred after arising and just before breakfast. Not all the attacks were accompanied by unconsciousness and convulsions, for occasionally they were very mild with mental confusion only. There was nothing of interest in his previous or family history. The general physical and neurologic examinations were essentially negative. Blood pressure 134/85.

Laboratory Data.—Urine negative. Blood: Leukocytes, 9,000; erythrocytes, 5,060,000; hemoglobin, 14.9 Gm. The differential count was normal and the blood Wassermann negative. The sugar tolerance curves, made September 29, 1934, and November 10, 1934, were low (Chart I). The maximum blood sugar was 100 mg. and the minimum 45 mg. per 100 cc. of blood. A diagnosis of possible hyperinsulinism was made and November 23, 1934, the abdomen was explored. Nothing pathologic was encountered and a subtotal pancreatectomy was performed, 22.5 Gm. of the gland being removed.

Pathologic Examination.—There were some areas of fat and pancreatic necrosis with leukocytic infiltration, showing them to be preoperative, which I am unable to explain. Some focal areas of necrosis without cell reaction may be postmortem. The island tissue was markedly swollen, edematous and congested. No tumors could be found. The islands were not particularly numerous and not noticeably increased in size. Impression: Hyperfunction of the Islands of Langerhans.

This patient made an uneventful convalescence but there was a recurrence of the seizures during the first month postoperatively. Chart 2 shows a steady diminution in the frequency of attacks during the 10 month period after operation but since December, 1935, the seizures have again become quite severe and are even more frequent now than before operation. A sugar tolerance test December 14, 1934, was still within the hypoglycemic zone in the first and second hours.

Case 3.—H. S., female, age 26, was admitted to the Firmin Desloge Hospital November 5, 1934, complaining of attacks of unconsciousness, pain in the lower abdomen and irregular menstruation. Her first convulsion was said to have occurred at the age of two. In successive years the seizures were infrequent until the advent of puberty, when they increased in frequency and severity. The attacks always occurred at the time of menstruation and were grand mal in type. They were generally preceded by an aura, the character of which she found impossible to describe. The patient has been married for four years. There was complete absence of libido. The menses were very irregular and the flow prolonged. About four months prior to admission she began to complain of

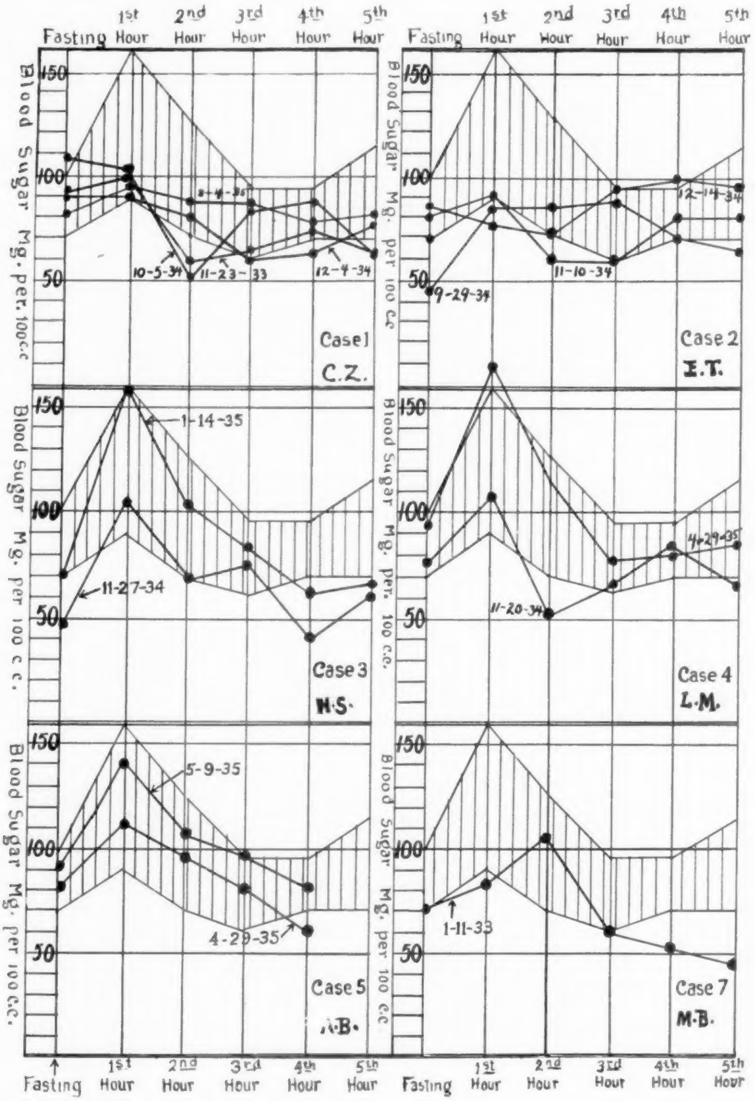

CHART 1.—Blood sugar determinations made before and after operation. The shaded area represents the zone for normal readings, by the Shaffer-Hartmann method. The earlier dates are preoperative, the later ones are postoperative.

pain, of a sharp stabbing character, occurring intermittently across the lower abdomen. This pain radiated both upwards and downwards and generally lasted for one-half to three-quarters of an hour. There were no previous illnesses of importance. The patient's mother suffered from epileptiform seizures which began at the age of 24 following a panhysterectomy.

The physical examination was negative except for moderate tenderness and muscle spasticity in the lower abdomen, particularly in the left lower quadrant. No definite masses could be felt. The pelvic examination revealed a second degree retroflexion with version and a first degree procedentia. Obesity prevented accurate palpation of the adnexa. A roentgenogram of the skull revealed an irregular, partly calcified shadow in the temporal region. Stereoscopic examination some days later failed to reveal this shadow but showed instead a condensation of bone in the inner table in the frontal region. It was felt, therefore, that there were not sufficient data from the roentgenologic standpoint to establish the diagnosis of a brain tumor. An ophthalmologic examination was negative and there were no abnormal neurologic findings. Ventriculograms did not show any definite indications of a cranial lesion.

Laboratory Data.—Urine, negative. Blood: Leukocytes, 6,800; erythrocytes, 4,570,000; hemoglobin, 13.2 Gm. Blood Wassermann, negative. A sugar tolerance curve made November 27, 1934, was low (Chart I). The maximum blood sugar was 104 mg. and the minimum 40 mg. per 100 cc. blood.

A diagnosis of questionable hyperinsulinism was made and on January 3, 1934, the abdomen was explored. Both ovaries were much larger and firmer than normal. The left was the larger, and measured 5 x 3 x 3 cm., and there was one very hard, nodular area at the inner pole. A piece was removed from this area for microscopic section. The kidneys and the abdominal aorta felt much smaller than one would normally expect. The pancreas presented no evidence of an adenoma, and the liver and adrenals appeared normal. Accordingly, a subtotal resection of the pancreas was performed, removing 40.2 Gm. This amount appeared to be approximately 80 per cent of the whole pancreatic mass.

Pathologic Examination.—The ovary shows extreme fibrosis with a few imprisoned cystic follicles. The lesion appears to be a benign neoplastic growth rather than an inflammatory mass. The pancreas itself exhibits no pathology.

The wound healed with some difficulty, as a fistula developed which drained for about two months before closing. The seizures continued after operation but the patient is insistent that they are less severe than previously. Chart 2 shows that the convulsive attacks occur with about the same frequency after operation as they did before. A sugar tolerance test, January 14, 1935 was within the hypoglycemic zone in the 4th and 5th hours.

Case 4.—L. M., male, age 27, was admitted to the hospital March 27, 1935 complaining of "fainting spells" which had begun seven years previously. These seizures, which were sometimes grand mal and at others petit mal in type, occurred from 10 to 15 times daily. Lately, they had been becoming more severe. His past and family histories were irrelevant. The physical examination was entirely negative, except for moderate tenderness on deep palpation in the right iliac fossa. The neurologic examination was also negative. Blood pressure 110/65.

Laboratory Data.—Urine, negative. Blood: Leukocytes, 9,600; erythrocytes, 4,850,000; hemoglobin, 85 per cent. The Kahn and Wassermann tests were negative. A sugar tolerance curve made November 20, 1934, was low (Chart I). The maximum blood sugar was 110 mg. and the minimum 52 mg. per 100 cc. of blood.

A diagnosis of possible hyperinsulinism was made and on March 28, 1935, the general abdomen and pancreas, in particular, were carefully explored. Nothing abnormal could be found. A subtotal pancreatectomy was performed, 23 Gm. of pancreatic tissue being removed.

Pathologic Examination.—The gross material consisted of 23 Gm. of pancreatic tissue. It was of light pink color and quite "meaty." It was of firm consistency throughout and had the "ropy" feel of the normal pancreas. Lobulation was quite evident, and these structures separated with little difficulty. There appeared to be no abnormal amount of fat associated with the gland. Small pieces were cut from the pancreas and fixed in Zenker's solution.

The paraffin technic was employed and sections were stained with hematoxylin-eosin as well as with Bensley's special stain for islet tissue granules. The microscopic examination of the sections stained with hematoxylin showed a slight fatty infiltration of the gland. The acini appear relatively exhausted of secretion. Generally speaking the islet tissue was pale and appeared to be vacuolated. The capillaries stood out strikingly, due to congestion. Some islet cells had giant nuclei. One section presented a rather large collection of islet tissue. This was quite distinctly set apart from the rest of the organ by slight, but definite, fibrous tissue encapsulation. The adenoma, when examined after special staining for granules, revealed both A and B types. The B type cells were much more numerous than the A. Only the one adenoma was found. Its location was in the tail of the pancreas (Figs. 1 and 2).

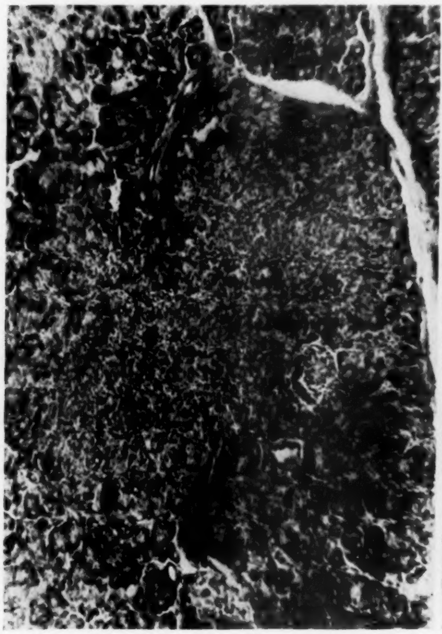

FIG. 1.—Low power photomicrograph showing the gross dimensions of the adenoma. A definite capsule may be noted. Compare size with that of adjacent normal islets and acini.

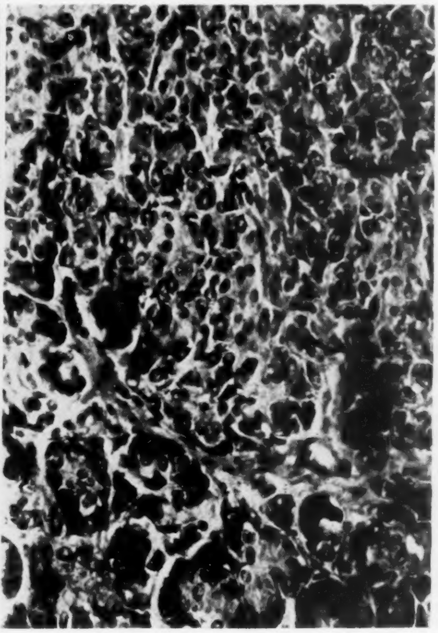

FIG. 2.—High power photomicrograph of the islet cell tumor showing the character of the cells. A portion of the capsule is seen. Special granule stains revealed both A and B cells, with the latter predominating.

Following operation there was an uneventful recovery except that there was a persistence of the convulsions. The patient was discharged from the hospital November 29, 1934. He was very uncooperative in carrying out the after treatment, particularly with reference to overindulgence in alcohol, and he appeared at the clinic from time to time complaining of seizures of greater frequency and intensity than before operation. Because of his general lack of cooperation with our after management on the outside, he was readmitted to the hospital October 21, 1935.

A second exploration of the pancreas was undertaken October 29, 1935, with the view of resecting more of the gland if possible. This was considered justifiable because of our previous finding of a small islet cell adenoma and because of the totally disabling nature of his disease.

An attempt was made to resect more of the gland but it was found too hazardous because of the dense fibrous adhesions which had incorporated the splenic vessels, inferior mesenteric vein and the distal end of the amputated pancreas en bloc. A large pale pinkish nodule lying between the head of the pancreas and the duodenum was identified by frozen section as a lymph node and not an adenoma. After an uneventful recovery the patient was discharged November 22, 1935. Since his second operation, the attacks, while no less frequent, are considerably milder. Chart 2 shows the relative frequency of convulsions before and since the first and second operations. Since January, 1935, the number of seizures per month has been greatly reduced, but recently (not shown on the Chart) they have recurred with the same intensity and frequency as before operation.

?, 1936

Case 5.—A. B., white, female, single, age 50, was admitted March 28, 1935, complaining of attacks of loss of consciousness with convulsions. She had had five major attacks since January 1, 1934, and seizures of minor character occurred almost daily For the past three years she has complained of vertigo brought on by any quick change of body position. In 1930, she was in an automobile accident and sustained a depressed fracture of the skull in the left frontal region, a fractured clavicle and fractures of several of the bones of the right hand. In 1931, an operation gave relief for pressure symptoms over the right eye of which she was complaining. With regard to her earlier medical history she stated that she had had cerebrospinal meningitis at the age of five, bronchopneumonia at 17 and in 1935 a nephropexy of the right kidney. In 1925, she had an hysterectomy, left oophorectomy and partial right oophorectomy and appendicectomy.

The physical examination was essentially negative. The scars of the previous operations were evident. The heart sounds were distant and the rhythm somewhat irregular with an occasional dropped beat. Blood pressure 115/65.

Laboratory Data.—Urine negative. Blood: Leukocyte and erythrocyte count and the hemoglobin estimation were normal. The Schilling differential was also normal. The sugar tolerance tests made April 29 and May 9, 1935, are shown in Chart 1. The maximum blood sugar was 140 mg. and the minimum 62 mg. per 100 cc. blood.

A presumptive diagnosis of hyperinsulinism was made and on May 22, 1935, the abdomen was explored. The adhesions of her former operations were so numerous that examination was directed toward the pancreas without further delay. The tail of the pancreas could not be mobilized nor adequately visualized because of its position (much farther to the left than I had previously encountered). The tip of the tail was attached by a fairly good-sized vascular pedicle high up under the left costal margin. To liberate it without more adequate exposure, which it did not appear possible to secure, seemed too dangerous inasmuch as a hemorrhage from this source had nearly proved fatal in a previous operation. Accordingly, a wedge of tissue weighing about 5 Gm., which had been devitalized and traumatized by the holding forcep, was resected and the abdomen closed with drainage.

Pathologic Examination.—The sections showed a moderate degree of fatty infiltration which was chiefly intralobular. There was some variation in the size of the acini, some being atrophic. The islet tissue was in rather large collections and was somewhat hyperplastic. It was not vacuolated, fibrous or hyalinized. The presence of hemorrhage was considered to be the result of operative trauma.

This patient subsequently developed a pancreatic fistula which will be reported elsewhere. In the 11 months' period following operation, there have been three convulsions of the major type but she states that she has been relieved entirely of her petit mal seizures. Chart 2 shows the frequency and severity of these hypoglycemic attacks before and since operation.

Case 6.—I. J., white, female, single, age 24, was admitted to the Firmin Desloge Hospital, May 11, 1935, complaining of abdominal pain and "epileptic fits." She had had these generalized convulsive attacks with loss of consciousness for nearly 20 years. They occurred every seven to ten days particularly just preceding or just following her menses. She had noted an aura. The attacks of abdominal pain which began at about the age of five were moderately severe and were confined to the umbilical region. They were frequently associated with the convulsive seizures. In childhood the attacks were far more frequent than they are at present.

The physical and neurologic examinations were essentially negative except for a slight tenderness on deep palpation over McBurney's point. There was no tenderness in the region of the navel and no masses could be felt anywhere. Blood pressure 130/79.

Laboratory Data.—Urine, negative. Blood: Leukocytes, 7,500; erythrocytes, 2,840,000; hemoglobin, 13.0 Gm. The Wassermann test was negative. A number of sugar tolerance tests were made and these revealed curves entirely within the normal zone. Roentgenologic examinations of the skull, gallbladder, esophagus and gastro-intestinal tract were all negative.

A diagnosis of chronic recurring appendicitis was made and on May 24, 1935, the appendix was removed through a right midrectus muscle splitting incision. The pancreas was exposed through the gastrocolic omentum and examined as well as possible, but no adenomata could be discovered. Pathologic examination of the appendix showed scarring, fatty changes and lymphoid hyperplasia with granulations and focal gatherings of round cells.

The patient made an entirely uneventful operative recovery. She was discharged June 10, 1935, but continued to have convulsions and attacks of abdominal pain precisely as before operation. She was readmitted December 18, 1935. Intravenous pyelograms were made to exclude possible renal or ureteral pathology. On reexamination of the abdomen it was still possible to elicit tenderness on deep palpation in both lower quadrants.

A presumptive diagnosis of hyperinsulinism was made on the basis of the convulsions and associated central abdominal pain and on December 20, 1935, the pancreas was exposed, through an upper left midrectus incision. A complete abdominal exploration revealed nothing pathologic. The pancreas was partially resected, removing 35 Gm. of tissue. Some difficulty was experienced with the dissection because of adhesions from the previous operation, but the gland was finally divided at a distance of 2.5 cm. from the duodenum.

Pathologic Examination.—The gross pancreas submitted for study was distinctly lobulated and the lobules separated with little difficulty. The gland substance appeared red rather than the more usual pink, but this seemed to be due to some hemorrhage within its substance. Only a slight amount of peripancreatic fat was seen.

Many small blocks from widely different areas were cut, fixed and stained with hematoxylin-eosin. All veins of the pancreas were noticeably engorged with blood. Hemorrhage was also found, particularly in the interlobular connective tissues. The congestion and hemorrhage were considered to be due to operative trauma. A slight fatty infiltration of the gland was noted. Generally speaking the ducts and acinar structures of the pancreas were not remarkable. Sections made from the tail of the organ show a very large number of islands, which would be expected. The capillaries in their substance are extremely prominent because of congestion which may again be due to necessary operative trauma. Many of the islands are rather strikingly large. This does not seem to be due to any exudative reaction, as there is no separation of the tissue by cellular or fluid exudate.

At one point, near the periphery of the pancreas, in a periductal position, are many large (microscopically) collections of islands. These are entirely set apart from the acini between them. The individual collections are surrounded with fibrous tissue. Cytologic study reveals normal islet tissue composing these collections.

The immediate course after operation was uneventful. The convulsive seizures continued but she states that they are less severe now than before operation. Chart 2 shows the same relative frequency of convulsive seizures before and since operation. The normal character of the blood sugar curves has not been altered. The attacks of abdominal pain were relieved temporarily but have lately recurred.

Case 7.—This patient did not come to operation but the opportunity of securing postmortem material in these cases is so unusual that we have included it in this series. Whipple reports only three necropsies in his group of 18 cases of hypoglycemia without tumors. Unfortunately, we did not receive the pituitary gland for study but it is particularly interesting to note that no definite lesions were found anywhere in the entire pancreas.

M. B., female, single, age 25, was admitted to the Firmin Desloge Hospital November 6, 1933. She complained of convulsive attacks which had begun at the age of 11. The description of the attacks given by relatives was that of a typical grand mal seizure. They seemed to increase in frequency at the time of her menses. There were no previous diseases of importance and no familial disorders. The physical examination was essentially negative; the neurologic examination was negative except that she appeared mentally retarded. Blood pressure 120/90.

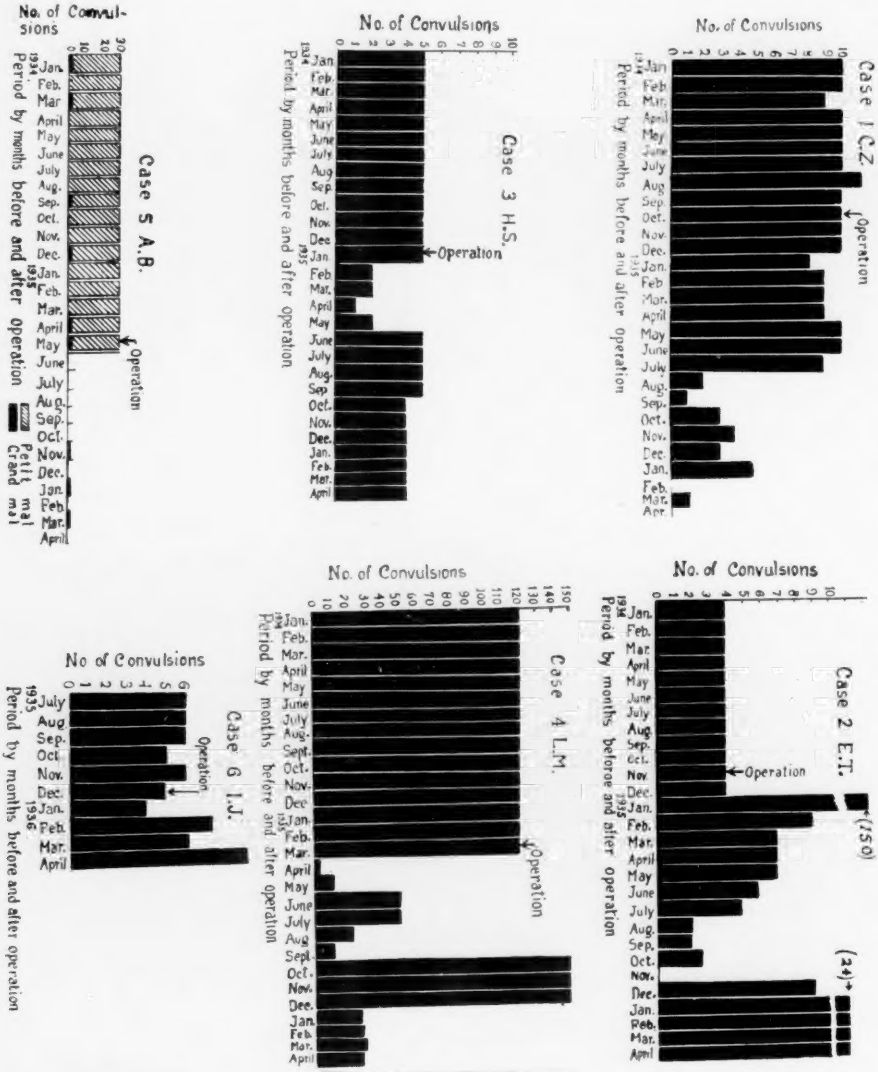

CHART 2.—Shows the frequency distribution of convulsions before and after operation.

Laboratory Data.—The blood and urine were negative. The Kahn test was negative The sugar tolerance test January 11, 1933, was low (Chart 2). The maximum blood sugar was 105 mg. and the minimum, 45 mg. per 100 cc.

She was discharged December 9, 1933, with a presumptive diagnosis of hyperinsulinism and advised to return to the Dispensary for observation and treatment. On November 6, 1934, she was urged to enter the hospital for a surgical exploration of the pancreas. She, however, fell in the street and received what appeared, at the time, to be a trivial head injury. She was put to bed immediately and died unexpectedly a few hours later. At a coroner's inquest, the cause of death was attributed to a linear fracture of the skull into the left orbital fossa with a subarachnoid hemorrhage. The pancreas was obtained and submitted to Dr. Collier for study.

Pathologic Examination.—A small accessory lobule was found in the pancreas near the junction of the body with the tail. The sections showed diffuse hypertrophy of the Islands of Langerhans. There were no adenomata anywhere in the gland.

Discussion.—The literature on the surgical treatment of hyperinsulinism has been reviewed and seven patients of our own, six of whom had had convulsive states associated with hypoglycemia, have been reported. Six of these patients were treated surgically by partial pancreatectomy. In only one patient did we find a tumor. In none of our six patients was there complete relief of the hypoglycemic convulsions, but there was some slight measure of improvement in three of the patients and none whatever in the remainder.

The surgical exploration of the pancreas, however, seems justifiable in those cases in which hypoglycemic sugar tolerance curves are found associated with frequent and severe convulsions which fail to respond at all to proper medical management. The incidence of hyperinsulinism particularly in its minor manifestations is far more common than has been supposed[3] but these patients may be dealt with satisfactorily by medical means. Unfortunately there is as yet no definite clinical method for differentiating hypoglycemic conditions which arise in the pancreas from those of extrapancreatic origin. Surgical exploration seems to be the only possible method of ascertaining the existence of adenomata and even this method is not altogether reliable as shown in Case 4, in which a very small adenoma of islet cells was discovered in the microscopic sections after the gross specimen had been reported normal.

The results in our series of patients were very unsatisfactory, as in not a single instance was a cure obtained. Nevertheless, our results are in keeping with the majority of the cases of resection of the pancreas for hyperinsulinism without tumors, reported in the literature. For example, in Whipple's collection of 18 cases with islet cell tumors removed at operation, 14 were completely free of symptoms after operation, three were improved and one patient had a malignant neoplasm and did not recover. On the other hand, in his 15 cases without tumor of the pancreas, the results were variable and much less favorable. In this latter group there was improvement or complete relief of symptoms in six patients and a persistence of the hypoglycemic convulsions, in six. One patient was still convalescing at the time of publication, in one the operation consisted only in a stripping of the capsule and in another a biopsy specimen was all that was obtained.

By way of contrast with the published results in the cases with tumors it will be noted that of 23 cases of hypoglycemic convulsions without tumors reported to date, in which a partial pancreatectomy was performed (Table I), eight were unrelieved, six were partially improved and in seven there was complete relief. One patient was convalescing at the time of report and another died of pneumonia three days postoperatively and therefore are not included in the table.

Analysis of these figures, Table II shows, for example, that it is practically impossible to correlate the amount of gland tissue resected with the postoperative results because the surgeons in six instances reported the amount removed either in fractions of the total length, in linear units or by anatomic designations such as "tail" or "tail and body," instead of in readily comparable units, such as the weight of the gland tissue resected. Neither may conclusions be drawn with regard to the pathologist's report for it would be necessary to assume that a painstaking examination of thin serial sections was made throughout the entire extent of the gross tissue and this does not seem probable.[8] Furthermore, we have already pointed out some of the difficulties encountered by pathologists in recognizing abnormal variations in size and number of islets.[1, 9]

In eight of the cases in which there was a persistence of the hypoglycemic symptoms and in which there was no evident improvement, the amount of gland removed varied from 5 to 35 Gm. In one case the amount was not mentioned. Of the seven cases in which the tissue had been weighed, the average weight was 16.3 Gm. The pathologic findings in these cases were normal pancreas in five, hypertrophy of the Islets of Langerhans in two and a small islet cell tumor in a normal pancreas in one.

In the six patients in which there was a persistence of the symptoms but who reported that their condition was improved in some degree, the amount of gland resected in five of them ranged from 5.0 to 40.2 Gm. In one case the operator reported the removal of 8 cm. of the pancreas but did not give the weight. The average weight of the five specimens was 17.8 Gm. The pathologic findings in four were normal and in one an hypertrophy of the Islands of Langerhans was noted and in another the islands seemed more numerous than normal.

In the seven patients with no return of the hypoglycemic syndrome after operation, the weight was given in only one case, *i.e.*, 60 Gm. In two cases one-half; in two cases, two-thirds, and in one, seven-eighths, of the gland was resected. In another the amount was represented as the "tail and body." In spite of the fact that the specific weight of the resected portion was given in but one case, it is quite probable that the average for this group would be considerably higher than that of the two preceding groups as the fractions of gland removed are in each instance given as one-half or more of the total gland. The pathologic findings reported in this group were normal pancreas in every instance.

Complete relief was therefore obtained in only one-third of the cases. This is not such a poor showing when the desperate condition of many of these totally incapacitated patients, as well as our ignorance of the etiologic

TABLE I

A REVIEW OF TWENTY-THREE CASES OF CONVULSIVE STATES ASSOCIATED WITH HYPOGLYCEMIA AND WITHOUT PANCREATIC ADENOMATA, SUBJECTED TO PARTIAL PANCREATECTOMY

(By Various Authors)

Case No.	Author	Reference to Publication	Age and Sex	Duration of Hypoglycemic Symptoms and Minimum Blood Sugar	Operation	Pathologic Examination	Results
1	Finney and Finney	Tr. Am. Surg. Assn., **46**, 268, 1928.	53—F.	4 yrs. 30 mg.	Resection of ⅔ or 22.5 Gm. of the pancreas	Apparently normal pancreas	Improved. Continues to have mild attacks. Blood sugar 45-70 mg.
2	Judd, *et al.*	J. A. M. A., **94**, 1116, 1930.	52—M.	2 yrs. 40 mg.	Resection of tail and part of body (14 Gm.)	Normal pancreas	Not improved 14 mos.
3	Judd, *et al.*	J. A. M. A., **94**, 1116, 1930.	47—M.	4 yrs. 40 mg.	Resection of 8 Gm. tail	Normal pancreas	Not improved 4 yrs.
4	Harris, S. (Taylor)	J. A. M. A., 1932.	20—M.	2 yrs. 50 mg.	Resection of tail and one-half of body	Normal pancreas	Improved: Blood sugar 17 mos. later was 100 mg.
5	Judd, *et al.*	J. A. M. A., **101**, 99, 1933.	50—M.	14 mos. 40 mg.	(1) May 25, 1931. Resection of 5 Gm. of tail of pancreas. (2) April, 1933. Portion of pancreas destroyed between clamps	Apparently normal pancreas	(1) Immediate improvement followed by recurrence of hypoglycemic attacks. (2) No improvement
6	(1) Holman and Railsback (2) Judd, Allan and Rynearson	Surg., Gynec., and Obst., **59**, 591, 1933.	31—M	1½ yrs. 32 mg.	(1) Resection of 8 cm. of tail, 1928. (2) Excision of nodule, 1932	(1) Apparently normal pancreas. (2) Chronic interstitial pancreatitis	(1) Improved though not entirely relieved of attacks. (2) Condition unchanged

TABLE I (*Continued*)

Case No.	Author	Reference to Publication	Age and Sex	Duration of Hypoglycemic Symptoms and Minimum Blood Sugar	Operation	Pathologic Examination	Results
7	Evans and McDonough	Jour. Iowa Med. Soc., **23**, 454, 1933.	41—F.	1 yr. (?) mg.	Amount resected unknown	Normal pancreas	Unimproved
8	Ziskind	Arch. Int. Med., **52**, 76, 1933.	19—M.	18 mos. 40 mg.	Resection tail 7.2 Gm.	Normal pancreas	Unimproved
9	Womack	1933 (personal communication)	35—M.	3 yrs. 40 mg.	Tail and part of body (⅔)	Normal pancreas	Remained symptom free
10	Womack	1933 (personal communication)	26—M.	3 yrs. 40 mg.	Tail and part of body (⅔)	Apparently normal pancreas	Improved—No recurrence hypoglycemic convulsions
11	Graham and Hartmann	Surg., Gynec., and Obst., **59**, 474, 1934.	12 mos.—F.	9 mos. 6 mg. "True Sugar"	Resection of ⅞ of the body and tail	Apparently normal pancreas	Remained well 9 mos.
12	Simon	South. Surg., **3**, 199, 1934.	26—M.	3½ mos. 51 mg.	Resection and destruction of approximately 60 Gm. of pancreas; gland appeared grossly enlarged	Islands of Langerhans enlarged	Recurrence of mild hypoglycemic symptoms for a short time
13	Thomason	(Personal communication), Western Surg. Assn., Dec. 8, 1934, St. Louis, Mo.	(?)—M.	(?) mos. 51 mg.	Subtotal pancreatectomy tail and body. Splenectomy	No adenoma	Improved, months (?)

14	Harris S. (Drennan)	South. Surg., **3**, 199, 1934.	32—F.	(?) 60 mg.	Subtotal ½ body and tail	Normal pancreas	No symptoms since operation (4 mos.)
15*	Harris, S. (Drennan)	South. Surg., **3**, 199, 1934.	27—M.	4 mos. (8 yrs.) 65 mg.	Excision ½ body and tail	Pancreatitis	No final report as patient convalescing
16	Berry, J. A.	Brit. Jour. Surg., **33**, 51, 1935.	58—F.	14 yrs. 45 mg.	Resection tail and part of body (28 Gm.)	Normal pancreas	Improved
17*	Barnes and Richmond	New Eng. Jour. Med., **213**, 225, 1935.	35—F.	18 mos. 30 mg.	Resection of 2 in. of the tail	Normal islet tissue chronic interstitial pancreatitis	Death from bronchopneumonia 3rd day postoperative
18	McCaughan and Broun	Case 1 (In press)	20—M.	3 yrs. 54 mg.	Resection of tail of pancreas (8 Gm.)	Number of Islands of Langerhans greatly increased but not abnormal	Some improvement. Resection of more pancreatic gland advised
19	McCaughan and Broun	Case 2 (In press)	17—M.	4 yrs. 36 mg.	Resection ⅔ body and tail of pancreas (22.5 Gm.) appeared grossly normal	Hypertrophy of the Islands of Langerhans	No improvement
20	McCaughan and Broun	Case 3 (In press)	26—F.	24 yrs. 25 mg.	Resection of 40.2 Gm. pancreas	Normal pancreas	Slightly improved. Severity of convulsions lessened
21	McCaughan and Broun	Case 4 (In press)	27—M.	7 yrs. 36 mg.	Resection of 23 Gm. pancreas	Islet cell. Tumor discovered in resected portion	Temporary improvement, then recurrence
22	McCaughan and Warner	Case 5 (In press)	50—F.	60 mg.	Resection of 5 Gm. pancreas	Normal pancreas	Slight improvement
23	McCaughan and Broun	Case 6 (In press)	24—F.	70 mg.	Resection of 35 Gm. pancreas	Hypertrophy of Islands of Langerhans	No improvement

* This case is not included in Table II.

factors responsible for the convulsive hypoglycemic syndrome, are taken into consideration.

TABLE II

AN ANALYSIS OF THE RESULTS OF PARTIAL PANCREATECTOMY IN TWENTY-ONE CASES OF CONVULSIONS WITH HYPOGLYCEMIA

Correlation of the results obtained, with amount of gland removed and with pathologic findings (Reported by Various Authors)

Postoperative Results	No. of Cases	Amount of Pancreas Resected	Pathologic Findings
No improvement	8	5.0 Gm. 7.2 Gm. 8.0 Gm. 14.0 Gm. 22.5 Gm.* 23.0 Gm.* 35.0 Gm.* (?) Gm.	Normal pancreas—5 cases. Normal pancreas with islet cell tumor—1 case.* Hypertrophy Islands of Langerhans—2 cases.**
		Average Weight 16.3 Gm.	
Improvement (some amelioration in the frequency and severity of hypoglycemic convulsions)	6	5.0 Gm.* 7.2 Gm. 8.0 Gm.* 28.0 Gm. 40.2 Gm.* 8.0 Gm.	Normal pancreas—4 cases.** No. of islands apparently increased—1 case.* Hypertrophy of Islands of Langerhans—1 case.
		Average Weight 17.8 Gm.	
Complete relief of symptoms	7	½ (tail and body) 2 cases ⅔ (tail and body) 2 cases ⅞ (tail and body) 1 case (?) (tail and body) 1 case 60 Gm. (tail and body) 1 case	Normal pancreas—7 cases.
		Average Weight (?) Gm.	

* Denotes cases in our own series.

CONCLUSIONS

Desperate cases of convulsive seizures associated with hypoglycemia unrelieved by proper dietary and medical treatment should be offered the opportunity afforded by surgical exploration. Adenomata if present may be removed with excellent prospects for cure. If no tumors are found, the pancreas can be partially extirpated without undue risk. The amount to be removed will depend upon the severity of the symptoms and the anatomic and pathologic conditions at hand. It is possible to remove the greater part of the human pancreas, apparently without serious disturbances to carbohydrate metabolism. If the pathologic findings in the resected portion show islet hypertrophy or small adenomata, a case improved by resection can be offered the benefit of additional resection if conditions are favorable for further operative procedure.

From a study of case reports in the literature it is evident that the end-results of operations in cases with islet cell tumors are excellent, and in patients without adenomata the results, while much less satisfactory, are occasionally gratifying. The results in our own particular series were very disappointing and should, we believe, dampen the enthusiasm of those who may be inclined to recommend surgery for the relief of any, and all, cases of hypoglycemia with nervous manifestations. It seems to us that until a positive method for differentiating cases of pancreatic adenomata from other functional abnormalities of the islet cells, particularly, those due to an imbalance between interrelated endocrines is developed, we will continue to meet with similar unfavorable results from subtotal resections of the pancreas. To add further to the general uncertainty and confusion in this field we have yet to mention that vast diagnostic dumping ground of vague and shadowy boundary—the group of so called idiopathic epilepsies.

To our mind the comparison of subtotal pancreatectomy for hyperinsulinism with the rationale of thyroidectomy for hyperthyroidism, as has been suggested by some, seems scarcely tenable in view of the uncertain and the generally unsatisfactory clinical results thus far reported in those cases without adenomata of islet cell origin.

REFERENCES

[1] Bensley, R. R.: Studies on the Pancreas of the Guinea Pig. Am. Jour. Anat., **12,** 297–388, 1911–1912.

[2] Berry, J. A.: A Case of Hyperinsulinism Relieved by Partial Pancreatectomy. Brit. Jour. Surg., **23,** 51–65, July, 1935.

[3] Coleman, J. M. A.: Study of Hypoglycemia with Particular Reference to Hyperinsulinism. Bull. St. Louis Med. Soc., **29,** 104, October 26, 1934.

[4] Harris, S.: Hyperinsulinism and Dysinsulinism. J.A.M.A., 729, September, 1924.

[5] Houssay, B. A., and Biasotti, A.: Hypophysis, Carbohydrate Metabolism and Diabetes. Endocrinology, **15,** 511–523, December, 1931.

[6] McCaughan, John M.: Subtotal pancreatectomy for Hyperinsulinism; Operative Technic. ANNALS OF SURGERY, **101,** 1336–1341, June, 1935.

[7] Parker, J. F., and Finley, C. S.: Some Results Obtained by Treatment of Nervous Phenomena with Glucose. Proc. Soc. Exper. Biol. and Med., **21,** 517, May, 1923–1924.

[8] Shields, W.: Adenomas of the Islands of Langerhans. Am. Jour. Path., **2,** 335–340, 1926.

[9] Thompson, W. R., Tennant, R., and Hussy, R.: Frequency-Distribution of Volume of Island of Langerhans in the Pancreas of Man, Monkey and Dog. Science, **78,** 270–271, September, 1933.

[10] Whipple, A. O., and Frantz, V. K.: Adenoma of Islet Cells with Hyperinsulinism; ANNALS OF SURGERY, **101,** 1299–1335, June, 1935.

[11] Wilder, R. M., Allen, F. N., Power, M. H., and Robertson, H. E.: Carcinoma of Island of Pancreas; Hyperinsulinism and Hypoglycemia. J.A.M.A., **89,** 348, July, 1927.

THE THYROID GLAND IN HYPOGLYCEMIA *

NATHAN A. WOMACK, M.D., AND WARREN H. COLE, M.D.
ST. LOUIS, MO.

FROM THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, AND THE ST. LOUIS CITY HOSPITAL NO. 1.

IN THE maintenance of body economy it is apparently necessary that the level of sugar in the blood should not be allowed to fall too low. When this does occur, either spontaneously or following the injection of insulin, certain clinical symptoms develop that have been explained as being due to a sudden excessive secretion of adrenalin. Our clinical experience in patients with spontaneous hypoglycemia has tended to confirm this observation on numerous occasions. Apparently, the action of adrenalin under such conditions is to mobilize sugar from the liver, so that the hypoglycemia can be relieved, and in so doing to produce other adrenalin effects in the body with ensuing clinical symptoms. That the adrenal medulla is not the only structure capable of producing an increased glycogenolysis is well known and will be discussed in detail subsequently. Certainly the thyroid gland has such a function and because of the fact that increased activity of the thyroid is generally associated with an increase in glycogenolysis, it has occurred to us that there may also be times in which it may be necessary for the body to utilize the secretion of the thyroid gland in hypoglycemia to maintain homeostasis. With this conception in mind the following case reports are presented.

CASE REPORTS

Case 1.—A. G., white, male, age 36, was admitted to the St. Louis City Hospital November 6, 1933, with the complaints of nervousness, tachycardia, dizziness and attacks of staggering while walking. His family and previous personal history were quite irrelevant other than that in 1917, following an attack of mumps, the right testicle underwent atrophy, and that he had contracted both gonorrhea and syphilis in 1920. Treatment for the latter was undoubtedly inadequate. He had been only an occasional user of alcohol, but is a heavy cigarette smoker and his consumption of coffee has been rather excessive.

Shortly after the World War the patient began to notice an increase in nervousness. This at first was extremely vague and the patient was unable to describe it accurately. It consisted for the most part in occasional dizzy spells and a sense of palpitation, none of which were severe enough to produce any incapacity. About four years before his admission into the hospital vague digestive disturbances began to appear, evidenced chiefly by constipation, distention and belching after meals. Shortly after this he began to have spells of smothering in which it was difficult to get his breath. This was followed by a marked increase in the frequency and degree of the attacks of dizziness. At times while walking, the patient would have such an attack during which he would stagger in a drunken fashion, not losing consciousness, but at the same time being completely disoriented. Palpitation became marked. During this time there was no history of girdle or shooting pains, neither was there any abnormality of gait.

---

* Read before the American Association for the Study of Goiter, Chicago, Ill., June 8, 1936. Submitted for publication July 13, 1936.

Physical Examination.—He seemed unusually restless. The pupils were normal and reacted to both light and accommodation. There was a slight exophthalmos which was associated with lid lag. A fine tremor of the tongue was present. The thyroid gland showed a definite diffuse enlargement; no nodules were palpable. The right testicle was atrophic. The rectal sphincter tone was normal. All reflexes were slightly exaggerated and a positive Babinski was present on the right side. The Gordon reflex and Oppenheim sign, however, were negative. A fine tremor was noted when the fingers were outstretched. The patient's hair was abundant and fine.

Laboratory Data.—The spinal fluid was found to be under normal tension. It contained six cells, and the colloidal gold determination was negative. The blood and spinal fluid Wassermann reaction was negative. The uranalysis was negative; the blood nonprotein nitrogen was 37 mg. per cent, hemoglobin 85 per cent and both red and white blood cell counts normal. Röentgenologic examinations of the skull showed a normal sella, and no evidences of increased intracranial pressure. Those of the chest likewise showed no abnormal findings. The basal metabolism on two determinations was +42 and +37 respectively.

Immediately following his first basal metabolism determination, he suddenly became disoriented and went into an attack of apparent automatic movements for about three minutes, after which he appeared normal. A blood sugar determination taken at this time (14 hours' fasting) showed it to be low. Sugar tolerance determinations following the ingestion of one gram of glucose per kilogram of body weight are shown in Table I.

TABLE I

RESULTS OF SUGAR TOLERANCE DETERMINATIONS

Fasting	30 Minutes	One Hour	Two Hours	Three Hours
72	117	96	72	62 (11/17/33)
66	133	100	71	47 (11/20/33)

Numerous fasting blood sugars ranged between 60 and 80 mg. per cent. All of these determinations were made according to the Folin-Wu method; the true sugar content would therefore be about 20 mg. per cent lower.

Rather than perform a thyroidectomy upon this patient, it was decided to explore the pancreas. The rationale for this decision will be considered in discussion of the case.

OPERATION.—November 11, 1933. Through a left rectus incision the pancreas was approached through the gastrocolic omentum. No gross abnormalities were found on its anterior surface. After freeing the inferior border, the gland was everted and the posterior surface likewise was found to be grossly normal. Exploration of the adrenal glands showed no evidence of enlargement, but this exploration, especially on the right side, was unsatisfactory. It was decided to perform a subtotal resection of the pancreas in order to remove some of the insulin secreting tissue. This was accomplished by removing the tail and most of the body. The stump of the pancreas was sutured over with a running chromic catgut suture and a drain carried down to the lesser sac through a stab wound. The abdominal wound was closed in layers. The postoperative course was uneventful. The drain was shortened after several days and upon its removal there was no fistula formation or any evidence of skin digestion.

PATHOLOGIC EXAMINATION.—*Gross*: The pancreas showed no evidence of tumor and the tissue appeared normal. *Microscopic* examination showed the islets to be normal in size, number, vacuolization, hyalinization and sinusoids. There was a very definite increase in the proportion of the alpha cells (Dr. James O'Leary).

POSTOPERATIVE COURSE.—The level of blood sugar remained elevated for several days, gradually coming down to normal. After about two weeks it became apparent that the thyroid gland was decreasing in size and the eye signs were beginning to recede. A basal metabolism determination at the time of the patient's discharge from the hospital on December 29, 1933, showed it to be zero. An examination to determine his sugar tolerance on January 10, 1934, gave the result as shown in Table II.

TABLE II

SUGAR TOLERANCE DETERMINATION TWO MONTHS POSTOPERATIVE

Fasting	30 Minutes	One Hour	Two Hours	Three Hours
80	190	235	173	80

The patient stated that most of the symptoms (including the manifestations of goiter) of which he complained had completely disappeared. No iodine medication of any kind was given either before or after operation. Since his operation about two and one-half years ago, the patient has been on relief and extremely difficult to follow. He was seen about two months ago, at which time he stated that there had been no return of his attacks, which we feel was explicable on the basis of his hypoglycemia. His thyroid was not enlarged. What his basal metabolic rate is and what his sugar tolerance curve is, however, we are unable to report upon.

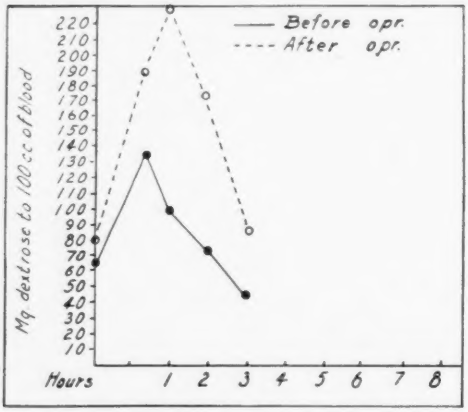

CHART 1.—(Case 1.) Showing graphically the sugar tolerance curves taken before partial resection of the pancreas and eight weeks after the operation.

For the privilege of presenting the second case we are indebted to Dr. S. H. Gray of the St. Louis Jewish Hospital. This case will be reported by him subsequently with others in greater detail, but because it presents morphologic evidence of the concept which we are suggesting, we are including it in our presentation.

Case 2.—An infant, born of an apparently normal mother, died about two hours after birth; it was comatose at birth and remained so until death. Upon autopsy the pancreas showed an extreme degree of hypertrophy and hyperplasia of the islet tissue (Fig. 1 A). The adrenal medulla as well as part of the cortex on both sides was completely destroyed by an old hemorrhage. (Fig. 1 B). The thyroid gland, instead of showing the usual picture of fetal thyroid, resembled that seen in Graves' disease to a marked extent (Fig. 1 C and D). Unfortunately, the hypophysis was lost. A notation made at autopsy, however, states that it was definitely enlarged.

The presence of compensatory hyperactivity of the thyroid is likewise suggested in a case recently under the care of Dr. L. F. Aitken[26] and which is being reported by him elsewhere. This patient, a married woman of 44, developed symptoms of amnesia, automatism, confusion and unconsciousness occurring before breakfast. Several months later she was said to have had a characteristic clinical picture of Graves' disease, the basal metabolic rate being plus 80 per cent. With the appearance of the hyperthyroidism the symptoms referable to hypoglycemia became less. A subtotal thyroidectomy was performed, following which the hypoglycemic symptoms increased in severity. After the removal of a *Beta* cell adenoma of the pancreas and the return to apparently normal carbohydrate metabolism, which was several years after the thyroidectomy, the patient developed evidence of hypothyroidism, and now requires one and one-half to two grains of desiccated thyroid per day.

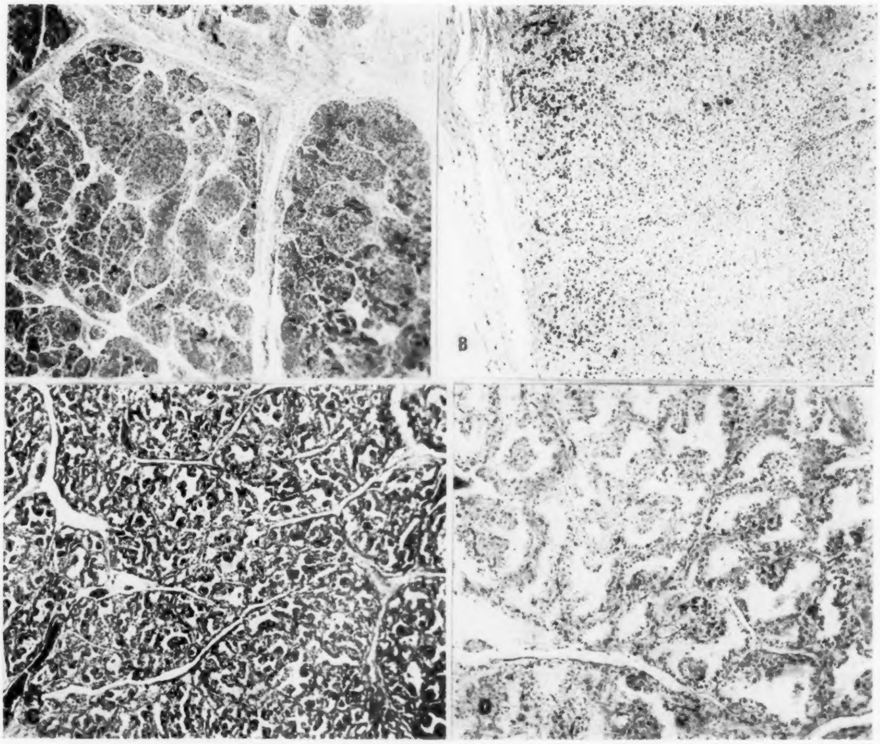

FIG. 1.—(Case 2.) Photomicrograph of the pancreas showing hypertrophy and hyperplasia of the islet tissue. (B) Photomicrograph of the adrenal gland showing the medulla completely destroyed by an old hemorrhage that is encroaching on the cortical layer. Both adrenals showed the same change. (C) Photomicrograph of the thyroid gland showing the general architecture. The loss of colloid, hyperplasia and plication of the epithelium may be seen (low power). (D) A higher power photomicrograph of the section shown in C. Morphologic evidence of increased thyroid activity is apparent.

For a number of years it has been suspected by many observers that the primary cause of toxic goiter is probably not to be found in the thyroid itself. It has been felt that the anatomic and physiologic changes brought about by the overfunction of this gland are the result of an unknown stimulus coming from some other part of the body. Indeed, such changes have already been produced experimentally by a varied group of substances. Perhaps the most striking is that which follows the injection of extracts from the anterior lobe of the pituitary gland.[1] We have observed such changes following certain types of infections[2] and toxemias and after the administration of some of the methylated purines.[3] Because of the dominant rôle that the thyroid plays in the fundamental activities of the body, it has appeared extremely important to us that this fact should not be lost sight of in studying the pathologic entity of toxic goiter. While the interrelationship of all the so called glands of internal secretion in their influence upon the metabolic processes of the body is becoming more and more apparent, especially is this true in carbohydrate metabolism and, although we feel that at the present time this effect is still poorly understood, it occurred to us that it would be of value to review some of the work on the action of the thyroid gland relative to sugar metabolism. The two cases that we have reported seem to us to illustrate a phase in the activity of the thyroid that we have never previously encountered clinically.

As early as 1867 Dumontpallier[4] called attention to the association of exophthalmic goiter with diabetes mellitus, and at that time expressed the opinion that this was not an accidental finding, but that a certain relationship may exist between the two. Since that time the association of these two diseases has been adequately confirmed by a number of authors, and various statistics as to its frequency have been quoted. These reports have differed markedly, and at times have appeared inconstant because of the failure to differentiate between true diabetes mellitus and the glycosuria that is seen so often in toxic thyroid disease. Recently, however, in a series of 25 cases of exophthalmic goiter, Anderson[5] has made a very comprehensive study of the subject. By the use of a special technic he was able "to demonstrate the presence of spontaneous glycosuria in every one (100 per cent)" of the 25 cases. All of these patients were on an "ordinary" diet. Likewise, in all of these patients he was able to show that after the ingestion of 70 grams of glucose, blood sugar determinations at ten minute intervals showed a higher and more protracted curve than that seen in normal individuals. In other reports glycosuria is not quite so frequent. John[6] found fasting glycosuria in only 19 per cent of the cases of hyperthyroidism. Joslin and Lahey[7] found the incidence somewhat greater. This subject was reviewed by Fitz[8] in 1921 and more recently by Andersen[9] in a detailed monograph. The incidence of hyperglycemia in hyperthyroidism, while generally showing a definite increase, likewise shows a marked variation. A number of reports on this aspect of the subject have been tabulated by John.[12]

Further evidence of this apparent lowering of carbohydrate tolerance by excessive thyroid function can be seen in the tendency of true diabetics to become worse following the development of toxic goiter. The reverse is true following thyroidectomy in these patients. While recognizing the difficulty in accurately estimating the amount of carbohydrate tolerance gained in diabetics with toxic thyroid disease after thyroidectomy, Joslin estimates it as "not far from 30 grams."[10] This type of improvement has been recognized and reported on by a number of other investigators including Fitz,[8] Wilder[11] and John. Similarly there is a tendency toward a lowered blood sugar in hypothyroidism, although in many instances clinical reports have been controversial, probably due to the interrelationship of other endocrine glands. Led by the observation that some diabetics seem to be improved following the development of myxedema, Wilder, Foster and Pemberton[13] have described a case of severe diabetes without evidence of hyperthyroidism upon whom a total thyroidectomy was performed with the production of hypothyroidism and a definite increase in sugar tolerance. This increase in tolerance seemed to parallel the decrease in metabolic rate. However, because of the unpleasant symptoms resulting from the myxedema, Wilder and his associates hesitated to recommend the procedure as a routine treatment. Shortly after their report a similar case was recorded by Rudy, Blumgart and Berlin,[14] in which a marked improvement in carbohydrate tolerance was noted following the total ablation of a normal thyroid gland in a severe diabetic. They were able to control the unpleasant symptoms of myxedema by small doses of thyroid extract, and are of the opinion that the procedure can be recommended in "the rare case with very severe diabetes which cannot be controlled adequately by the application of all known therapeutic measures."

From a study of the above clinical reports and others of the same type, it seems justifiable to conclude that in patients with hyperfunction and hypofunction of the thyroid gland there is clinical evidence of alteration of the tolerance to glucose in the body.

Experimentally, the evidence is even more conclusive. As early as 1904 Lorand[15] reported that ten days after thyroidectomy in dogs made diabetic by previous pancreatectomy there was a disappearance of the glycosuria. This experiment was repeated by Eppinger, Falta and Rudinger[16] and subsequently by W. G. MacCallum[17] with results of a similar nature but not so striking. They were able to obtain a diminution of the glycosuria, but not a complete disappearance. More recently, however, Yriat[27] has failed to confirm such findings. In an effort to explain this phenomenon the first important contribution was that by Cramer and Krause[18] who, in 1913, showed that the feeding of thyroid substance to cats and rats resulted in a diminution in the amount of glycogen in the liver. This finding has been confirmed by others on numerous occasions. Lichtman[19] has used it as a basis of explaining the occasional clinical evidence of hepatic disease in severe cases of hyperthyroidism. By the use of a functional test based on the ability of the liver to oxidize cinchophen he was able to show a disturbance in function in 16 of 20 cases of uncomplicated hyperthyroidism. "There was no apparent relationship between the degree of functional impairment of the liver and the basal metabolic rate, the known duration of the disease or the percentage of weight lost. . . . The constancy of depletion of glycogen in the liver cells in animals that have been fed thyroid substance, and probably in clinical thyrotoxicosis suggests that the disturbance in oxidation of cinchophen is related to the capacity of the cells to store and mobilize glycogen." Youmans and Warfield,[20] using the phenoltetrachlorphthalein test, found an impairment of hepatic function in 50 per cent of their cases and concluded that "it is probable therefore that a change in thyroid activity in thyrotoxicosis may result in a glycogen free or poor liver, more susceptible to damage by some toxic agent present in this disease or more susceptible to injury by the disturbed thyroid function itself." In an extensive study of the morphologic changes in the liver in Graves' disease, Weller[21] was able to show definite damage in 54 per cent of a group of selected cases, while in a matched control series the frequency was only 2 per cent. A similar study by Beaver and Pemberton[22] describes three predominant types of hepatic lesions in exophthalmic goiter: (1) acute degenerative lesions; (2) simple atrophy; and (3) subacute toxic atrophy and toxic cirrhosis.

Burn and Marks,[23] in 1925, while studying the relation of the thyroid gland to the action of insulin, noted that "the presence of large amounts of thyroid hormone in the circulation enables the organism to prevent the occurrence of severe hypoglycemia in spite of the injection of relatively large doses of insulin." This observation was found to be true until the liver had been depleted completely of available glycogen and was thought to be explained by the action of the thyroid in stimulating glycogenesis. Recently, Goldblatt[24] has observed that in many instances when an apparent sensitivity to insulin has existed, the underlying factor has been an inability on the part of the organism to mobilize sugar readily from the liver to replenish the falling level in the blood stream. Such an explanation would suffice in the insulin sensitivity seen following removal of the adrenals. In the recent work of Cope and Marks,[25] a similar explanation of the insulin sensitivity following hypophysectomy may be given. These workers have developed the conception that the effect of adrenalin on glycogenolysis depends upon the presence of the anterior lobe of the hypophysis. Through hormonal secretion this structure apparently possesses the ability to mobilize liver glycogen, and is stimulated to do so by the presence of adrenalin. Without the presence of the anterior lobe of the hypophysis, adrenalin loses its ability to free the liver of sugar, and the reaction to a small dose of insulin becomes much more marked.

The presence of an increased sensitivity to insulin in myxedema and in the thyroidectomized animal has been known to exist for a long time. Goldblatt has shown that the response to adrenalin in the thyroidectomized animal is both slower in onset and less in degree in so far as the blood sugar determinations are concerned. He is of the opinion that lack of thyroid secretion produces a "failure to initiate adequate glycogenolysis at the hypoglycemic blood sugar levels" and that this is due to "the sluggishness of response of the sympathetic mechanism responsible for glycogenolysis in the liver."

From the above studies, therefore, it seems apparent that the thyroid secretion is capable of elevating the level of sugar in the blood with the potential production of glycosuria. It depletes the liver of glycogen and tends to make the body more resistant to the action of insulin. While these effects may be due partly to the increase in the utilization of glucose caused by an increase in the amount of oxidation in the body, they probably are best explained by the marked effect of the thyroid secretion in producing more rapid glycogenolysis. Such an action as has been shown on repeated occasions occurs quite dramatically when the adrenal-sympathetic mechanism is stimulated. With the presence of a similar function in the thyroid gland we are apparently dealing with a balanced physiologic synergy in which three different structures act toward the same end, enhancing the action of each other. They all tend to elevate the blood sugar level. Such a statement, however, should not be construed to mean that these structures do not likewise exert an action independent of each other.

Discussion.—While differing in degree, it is apparent that the thyroid, as well as the adrenal-sympathetic system, acts in effecting the mobilization of glycogen from the liver. It is only by the utilization of such a complex mechanism that the organism is able to preserve the blood sugar at the constant level obviously necessary in the economy of the body. During phases of acute hypoglycemia, occurring spontaneously or induced by insulin, the most important factor in restoring the sugar to the normal level in all probability is the adrenal gland. Certainly there is considerable experimental and clinical evidence in support of this. However, it seems reasonable to believe that if for some reason this mechanism were altered so that the adrenal action was insufficient, the thyroid gland might compensate by increasing its functional activity. The two cases described above suggest that this is true. If the evidence of increased thyroid activity noted in the first case were of a compensatory nature, we cannot help but feel that thyroidectomy would only tend to aggravate the symptoms of hypoglycemia. It is for this reason that pancreatic resection was advised. It is only fair to state that in our opinion such a situation is rare. Certainly, in our experience, this is the first patient that we have encountered with a blood sugar consistently low and severe enough to produce symptoms associated with a toxic goiter. However, we do wish to emphasize one thing. The presence of a goiter and signs of hyperthyroidism are not necessarily indications for thyroidectomy until detailed study offers evidence that this is the best treatment. Until this is done the clinician can hope to contribute but little to the solution of the problem of Graves' disease.

CONCLUSIONS

(1) Evidence of the effect of the thyroid gland on carbohydrate metabolism is briefly reviewed.

(2) The action of the thyroid secretion in mobilization of sugar from the liver is considered in detail.

(3) Evidence is brought forward to show that because of this action the thyroid gland may undergo compensatory hyperactivity in occasional hypoglycemic states in an effort to elevate the level of sugar in the blood.

(4) Two cases are presented, one of which shows clinical evidence and

the other morphologic evidence of such compensatory hyperactivity of the thyroid. In the first case the presence of the classical features of Graves' disease was noted.

(5) In one of these cases an apparent toxic goiter disappeared following the relief of the hypoglycemia after partial resection of the pancreas.

REFERENCES

[1] Loeb, Leo, and Bassett, R. B.: Proc. Soc. Exper. Biol. & Med., **26**, 860, 1929.

[2] Cole, W. H., and Womack, N. A.: J. A. M. A., **90**, 1274, 1928.

[3] Cole, W. H., Womack, N. A., and Ellet, M.: Arch. Surg., **22**, 926, 1931.

[4] Dumontpallier: Compt. rend. Soc. de biol., **19**, 116, 1867.

[5] Anderson, W. T.: Acta med. Scandinav. **78**, 229, 1932.

[6] John, H. F.: J. A. M. A., **99**, 620, 1932.

[7] Joslin and Lahey: Am. J. M. Sc., **176**, 1, 1928.

[8] Fitz: Arch. Int. Med., **27**, 305, 1921.

[9] Andersen, W. T.: Studies on Blood Sugar and Glycosuria in Exophthalmic Goiter. Levin and Munksgaard, Copenhagen, 1933.

[10] Joslin: Treatment of Diabetes Mellitus. Lea and Febiger, Philadelphia, 1935.

[11] Wilder, R. M.: Arch. Int. Med., **38**, 736, 1926.

[12] John, H. F.: Endocrinology, **11**, 497, 1927.

[13] Wilder, R. M., Foster, R. F., and Pemberton, J. de J.: Proc. Staff Meet., Mayo Clin. **8**, 720, 1933.

[14] Rudy, A., Blumgart, H. L., and Berlin, D. D.: Am. J. M. Sc., **190**, No. 1, 51, 1935.

[15] Lorand, A.: Compt. rend. Soc. de biol., **56**, 488, 1904.

[16] Eppinger, H. W., Falta and Rudinger, C.: Ztschr. f. klin. Med., **66**, 1, 1908.

[17] MacCallum, W. G.: Bull. Johns Hopkins Hosp., **20**, 265, 1909.

[18] Cramer and Krause: Proc. Royal Soc., Series B., **86**, 550, 1913.

[19] Lichtman, S. S.: Arch. Int. Med., **50**, 721, 1932.

[20] Youmans, J. B., and Warfield, L. M.: Arch. Int. Med., **37**, 1, 1926.

[21] Weller, C. V.: Ann. Int. Med., **7**, 543, 1933.

[22] Beaver, D. C., and Pemberton, J. de J.: Ann. Int. Med., **7**, 687, 1933.

[23] Burn, J. H., and Marks, H. P.: J. Physiol. **60**, 131, 1925.

[24] Goldblatt, M. W.: J. Physiol., **86**, 46, 1936.

[25] Cope, O., and Marks, H. P.: J. Physiol. **83**, 157, 1934.

[26] Aitken, L. F.: Personal communication.

[27] Yriat, M.: Compt. rend. Soc. de biol., **105**, 128, 1930.

THE VARIATIONS OF BLOOD AMYLASE DURING ACUTE TRANSIENT DISEASE OF THE PANCREAS

ROBERT ELMAN, M.D.

ST. LOUIS, MO.

FROM THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, THE BARNES AND ST. LOUIS CITY HOSPITALS, ST. LOUIS, MO.

A SERIES of observations is recorded on patients suffering severe, but transient, attacks of acute epigastric pain during which the blood was studied for its content of amylase, a starch-splitting ferment which is present in the pancreatic juice, circulating blood, and elsewhere. The findings seemed to indicate such a definite relationship between the alterations in the blood amylase and the condition of the pancreas as to be of considerable diagnostic value. Since disease of the pancreas is so difficult to detect on clinical examination alone, the importance of blood amylase determinations is obvious.

PREVIOUS OBSERVATIONS.—In previous papers[1, 2] from this clinic the value of blood amylase determinations in the detection of acute pancreatic disease was discussed. However, only single determinations of the ferment were made; this, indeed, is true of nearly all of the clinical studies which one finds in the literature. The repeated measurement, day after day, as the clinical manifestations change has not been made. In recent years, particularly, but few clinical studies of blood amylase have been recorded. Acute pancreatic necrosis is such a rare condition that surgeons have perhaps not been impressed with the necessity of a laboratory test for its recognition. In other studies from this clinic[3, 4] however, it was suggested that acute pancreatitis without necrosis, and of a transient nature, was perhaps a frequent condition, often masquerading as biliary colic, peptic ulcer or intestinal obstruction. If so, blood amylase determinations should be made more frequently. It is of special interest to note that E. A. Graham,[5] over ten years ago, stated: "Is it not probable that many cases of severe epigastric pain of uncertain nature which clear up spontaneously are of this origin?" (*i.e.*, acute pancreatitis). A recent publication by Comfort,[6] from the Mayo Clinic, has also indicated the probable frequency of acute pancreatic disease; instead of blood amylase this observer measured blood lipase, a ferment also present in the pancreatic juice. He found that there was an increased lipase content of the blood in 17 of 20 patients in whom the clinical and pathologic data pointed to an acute process. The blood was examined within ten days after the onset of the acute attack of the upper abdominal disease or during a period of persisting symptoms. In each case the surgeon reported the presence of pancreatic disease at subsequent operation.

The origin of the starch-splitting ferment, amylase, found in the blood, has been the subject of much dispute, although, as already pointed out,[1] the bulk of

---

Submitted for publication June 1, 1936.

the other morphologic evidence of such compensatory hyperactivity of the thyroid. In the first case the presence of the classical features of Graves' disease was noted.

(5) In one of these cases an apparent toxic goiter disappeared following the relief of the hypoglycemia after partial resection of the pancreas.

REFERENCES

[1] Loeb, Leo, and Bassett, R. B.: Proc. Soc. Exper. Biol. & Med., **26,** 860, 1929.
[2] Cole, W. H., and Womack, N. A.: J. A. M. A., **90,** 1274, 1928.
[3] Cole, W. H., Womack, N. A., and Ellet, M.: Arch. Surg., **22,** 926, 1931.
[4] Dumontpallier: Compt. rend. Soc. de biol., **19,** 116, 1867.
[5] Anderson, W. T.: Acta med. Scandinav. **78,** 229, 1932.
[6] John, H. F.: J. A. M. A., **99,** 620, 1932.
[7] Joslin and Lahey: Am. J. M. Sc., **176,** 1, 1928.
[8] Fitz: Arch. Int. Med., **27,** 305, 1921.
[9] Andersen, W. T.: Studies on Blood Sugar and Glycosuria in Exophthalmic Goiter. Levin and Munksgaard, Copenhagen, 1933.
[10] Joslin: Treatment of Diabetes Mellitus. Lea and Febiger, Philadelphia, 1935.
[11] Wilder, R. M.: Arch. Int. Med., **38,** 736, 1926.
[12] John, H. F.: Endocrinology, **11,** 497, 1927.
[13] Wilder, R. M., Foster, R. F., and Pemberton, J. de J.: Proc. Staff Meet., Mayo Clin. **8,** 720, 1933.
[14] Rudy, A., Blumgart, H. L., and Berlin, D. D.: Am. J. M. Sc., **190,** No. 1, 51, 1935.
[15] Lorand, A.: Compt. rend. Soc. de biol., **56,** 488, 1904.
[16] Eppinger, H. W., Falta and Rudinger, C.: Ztschr. f. klin. Med., **66,** 1, 1908.
[17] MacCallum, W. G.: Bull. Johns Hopkins Hosp., **20,** 265, 1909.
[18] Cramer and Krause: Proc. Royal Soc., Series B., **86,** 550, 1913.
[19] Lichtman, S. S.: Arch. Int. Med., **50,** 721, 1932.
[20] Youmans, J. B., and Warfield, L. M.: Arch. Int. Med., **37,** 1, 1926.
[21] Weller, C. V.: Ann. Int. Med., **7,** 543, 1933.
[22] Beaver, D. C., and Pemberton, J. de J.: Ann. Int. Med., **7,** 687, 1933.
[23] Burn, J. H., and Marks, H. P.: J. Physiol. **60,** 131, 1925.
[24] Goldblatt, M. W.: J. Physiol., **86,** 46, 1936.
[25] Cope, O., and Marks, H. P.: J. Physiol. **83,** 157, 1934.
[26] Aitken, L. F.: Personal communication.
[27] Yriat, M.: Compt. rend. Soc. de biol., **105,** 128, 1930.

THE VARIATIONS OF BLOOD AMYLASE DURING ACUTE TRANSIENT DISEASE OF THE PANCREAS

ROBERT ELMAN, M.D.
ST. LOUIS, MO.

FROM THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, THE BARNES AND ST. LOUIS CITY HOSPITALS, ST. LOUIS, MO.

A SERIES of observations is recorded on patients suffering severe, but transient, attacks of acute epigastric pain during which the blood was studied for its content of amylase, a starch-splitting ferment which is present in the pancreatic juice, circulating blood, and elsewhere. The findings seemed to indicate such a definite relationship between the alterations in the blood amylase and the condition of the pancreas as to be of considerable diagnostic value. Since disease of the pancreas is so difficult to detect on clinical examination alone, the importance of blood amylase determinations is obvious.

PREVIOUS OBSERVATIONS.—In previous papers[1, 2] from this clinic the value of blood amylase determinations in the detection of acute pancreatic disease was discussed. However, only single determinations of the ferment were made; this, indeed, is true of nearly all of the clinical studies which one finds in the literature. The repeated measurement, day after day, as the clinical manifestations change has not been made. In recent years, particularly, but few clinical studies of blood amylase have been recorded. Acute pancreatic necrosis is such a rare condition that surgeons have perhaps not been impressed with the necessity of a laboratory test for its recognition. In other studies from this clinic[3, 4] however, it was suggested that acute pancreatitis without necrosis, and of a transient nature, was perhaps a frequent condition, often masquerading as biliary colic, peptic ulcer or intestinal obstruction. If so, blood amylase determinations should be made more frequently. It is of special interest to note that E. A. Graham,[5] over ten years ago, stated: "Is it not probable that many cases of severe epigastric pain of uncertain nature which clear up spontaneously are of this origin?" (*i.e.*, acute pancreatitis). A recent publication by Comfort,[6] from the Mayo Clinic, has also indicated the probable frequency of acute pancreatic disease; instead of blood amylase this observer measured blood lipase, a ferment also present in the pancreatic juice. He found that there was an increased lipase content of the blood in 17 of 20 patients in whom the clinical and pathologic data pointed to an acute process. The blood was examined within ten days after the onset of the acute attack of the upper abdominal disease or during a period of persisting symptoms. In each case the surgeon reported the presence of pancreatic disease at subsequent operation.

The origin of the starch-splitting ferment, amylase, found in the blood, has been the subject of much dispute, although, as already pointed out,[1] the bulk of

---

Submitted for publication June 1, 1936.

the evidence indicates that it is of pancreatic origin, in large part at least. The question has more than theoretical interest in so far as it concerns the significance of changes in blood amylase in relation to the presence or absence of pancreatic disease. Doubtless the final answer to the question of the origin of blood amylase will be made after further experimental study. For the present, observations recorded herein will be concerned only with the practical and diagnostic, not with the etiologic correlation, of blood amylase and the pancreas.

Method.—A discussion of the various methods for the measurement of amylase may be found elsewhere.[1] In general, three main types of procedure are available for the detection of this enzyme. The oldest is based on the disappearance of starch in suspension as shown by the starch-iodine test; this method has been popularized by Wohlgemuth. The second procedure is based on the measurement of the glucose produced by the ferment acting on starch, called conveniently the sugar reduction method. The third or viscosimetric technic depends upon the reduction in the viscosity of a colloidal starch solution as digestion proceeds.

In the present study blood amylase was studied by one or the other of all three methods. The values found were so high that the differences in method played no rôle in the findings. While the viscosimetric method, as reported in previous papers is probably the most accurate, it requires more care and equipment than is essential in measuring the high values herein reported. For detecting high concentrations of amylase, therefore, any of the three methods suffice and indeed the simplest is most advisable. Undoubtedly the sugar reduction technic is best adapted for use in most clinical laboratories. Descriptions of the various methods will be found in text-books on clinical laboratory technic. A modified sugar reduction method which is used in many Saint Louis hospitals has been devised by Dr. Michael Somogyi and is carried out as follows:

A colloidal suspension of 1½ per cent washed (C.P.) corn starch is prepared as a starch solution, which if sterile keeps fairly well; the formation of molds makes it unsuitable. To 5 cc. of this suspension, 1 cc. of the patient's plasma or serum and 2 cc. of 1 per cent sodium chloride is added, and the mixture incubated for 30 minutes at 40° C. Then 1 cc. of 5 per cent $CuSO_4$ is added immediately, the mixture is shaken and 1 cc. of 7 per cent sodium tungstate is added; the mixture is again shaken and filtered. Sugar determination is made on 5 cc. of the filtrate. From the total amount of sugar formed by the hydrolysis of the starch, is subtracted the amount of sugar present in 1 cc. of the patient's serum. The result is expressed in milligrams of sugar per 100 cc. of blood. Normally 70 to 200 milligrams of sugar will be produced by 100 cc. of blood serum in this way. At the height of an acute pancreatic obstruction or inflammation this value may reach a figure as high as 3,000 mg. (*i.e.*, mg. per 100 cc. of blood).

COMMENT.—Eight cases are recorded of patients suffering acute epigastric pain of short duration, during which the blood amylase, extremely high during the height of symptoms, gradually returned to normal with the subsidence of the attack. The main clinical findings are summarized in Table I. The blood amylase values of seven of the cases are represented in Chart 1, and of the eighth case in Chart 2.

TABLE I

Patient	Sex, Age	Duration of Attack (days)	Cholecystogram	Jaundice	Clinical Diagnosis	Remarks
No. 1....	F. 29	3	Faint shadow	++	Biliary colic	Refused operation; many similar previous attacks. High dye retention.
No. 2.....	F. 35	3	No shadow	+	Biliary colic	Cholecystectomy 3 days after attack. Fat necrosis of pancreas. (Biopsy)
No. 3....	F. 32	3	No shadow	+	Acute interstitial pancreatitis	Recurrent attack: cholecystectomy 2 mos. previously
No. 4....	F. 43	2	No shadow	+++	Ruptured peptic ulcer	Cholecystectomy 14 days after attack, stone; biopsy of pancreas normal; head of pancreas indurated
No. 5....	F. 34	4	Normal	+	Biliary colic	Cholecystectomy 1 wk. after attack. Chronic inflamed gallbladder containing stones, firm pancreas by palpation
No. 6....	F. 28	2	Good shadow with several nonopaque stones	0	Biliary colic	Cholecystectomy 1 wk. after attack; pancreas firm to palpation
Nc. 7....	M. 37	3	Faint shadow (subsequently normal)	0	Intestinal obstruction	Similar attacks previously; local tenderness over pancreas; no operation
No. 8....	F. 42	1	Not taken	++	Coronary disease	History of repeated attacks diagnosed biliary colic. Chronically inflamed gallbladder with stones removed before present attacks (see chart 2)

The correlation between the clinical behavior of the patients and the content of amylase in the blood was striking. In four cases a laparotomy was performed after the attack had subsided. In all of them the pancreas was palpated and found to be firm and indurated. In each patient a diseased gall-bladder containing stones was found and removed. In one of them operation was performed three days after the attack, and the pancreas was inspected and found to contain areas of fat necrosis about it and a biopsy revealed interstitial pancreatitis. Biopsy of the pancreas in another patient revealed no microscopic change even though the gland felt hard and indurated; operation, however, was performed two weeks after the attack had subsided. In the remaining four patients the evidence of pancreatic disease was based on the high amylase values, although all had similar clinical manifestations of severe epigastric pain, nausea, vomiting, *etc.* Of the four cases, however, two had already had a cholecystectomy; they represented therefore examples of recurrent pain.

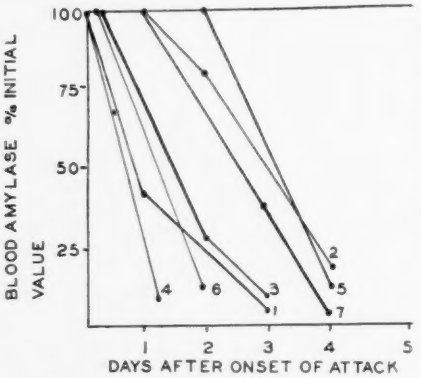

Chart 1.—Composite graph of blood amylase values in seven cases of transient epigastric pain, *etc.* (see Table 1).

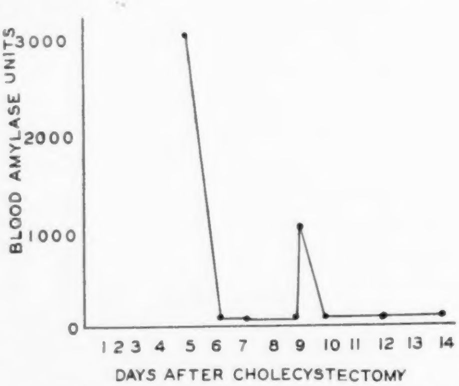

Chart 2.—Graph of blood amylase values in case 8 (Table 1). The two attacks on the sixth and ninth postoperative days simulated coronary disease.

Although the number of cases is small, the evidence presented suggests that acute pancreatic disease may prove to be the cause of many attacks of upper abdominal pain which have hitherto been usually diagnosed as biliary colic, but in certain instances perforated ulcer, intestinal obstruction or coronary disease. The behavior of the blood amylase in these cases is striking and certainly warrants the use of this test in patients with manifestations of acute upper abdominal disease. Further study will undoubtedly reveal the nature of the pancreatic lesion which probably accounts for the rise and fall of the blood amylase. Previous reports have recorded the existence of many instances similar, clinically, to the present cases, in which the presence of acute interstitial pancreatitis was described. Fat necrosis in the region of the pancreas was also noted in some of these cases. It may be, however, that in certain instances the lesion responsible for the rise and fall of blood amylase is merely a transient obstruction to the main pancreatic duct; actual parenchymatous inflammation may not be necessary to explain the clinical and laboratory findings. Indeed, unless the pancreas is observed at the time of acute symptoms, no abnormality may be expected if the lesion is of a transient nature. This may be the explanation of the normal findings in the biopsy of the pancreas in Case 4. On the other hand, the disease may be confined to the head of the pancreas; biopsy of other portions of the gland may thus be normal. The localization of the inflammation to the head of the pancreas is suggested by its frequency, as observed by a great many surgeons. Experimental evidence has repeatedly shown how rapidly, and how extensively, blood amylase will rise after the production of pancreatic disease, particularly duct obstruction. Recent studies of this type have been reported by Clasen, Johnstone and Orr[7] and by McCaughan.[8] However, there is no evidence that increases in blood amylase ever occur except when pancreatic disease is present.

It is suggested, as a fruitful source of further study, that when possible estimations of blood amylase at frequent intervals be made on all patients with severe, acute, upper abdominal pain from the very onset of the attack. When operations are performed upon such patients, particularly those with biliary disease, the pancreas should not only be palpated in order to detect enlargement and induration but also inspected particularly for the existence of fat necrosis. In many patients operated upon within a week or two of the attack the latter finding may be expected inasmuch as it takes some time for the evidences of fat necrosis to disappear. Biopsy, finally, of the pancreas, particularly when induration and swelling is present, will often reveal objective data as to the nature of the lesion, provided, however, operation is carried out during or within a day or two after the attack. The probable frequency of hitherto unsuspected pancreatic disease capable of producing severe symptoms will thus be established. The practical importance of such observations concerns, in part, the problem of recurrent pain after cholecystectomy; such a distressing sequela to operation is often due to pancreatic disease.[4] Case 3 in the present series represents such an instance.

It should be emphasized that the present findings are not concerned with acute pancreatic necrosis, a disease which behaves quite differently. While this lesion is accompanied by elevation of the blood amylase it rarely, if ever, subsides spontaneously; in most instances the progress of the patient is steadily downward. When the patient is suffering from pancreatic necrosis the existence of serious manifestations of circulatory impairment, such as low blood pressure, rapid thready pulse, and cyanosis are sufficiently characteristic to differentiate the disease from simple subsiding pancreatitis. The blood amylase in two cases of pancreatic necrosis was recently studied, and in them a very high value was found which decreased slowly, reaching a subnormal level just before death. Operation had not been performed in either case. At autopsy the pancreas, in each instance, was found to be completely destroyed, thus accounting for the fall of blood amylase. The significance of the fall of blood amylase in such a case is obviously quite different from those described in detail above. It is clear, therefore, that while a high amylase points to the existence of serious pancreatic disease, the decision as to operation, based on the presence or absence of pancreatic necrosis, must be made on other grounds.

From the evidence now available one may only say that the blood amylase reflects the existence of, but does not reveal, the nature of a pancreatic lesion. On the other hand, the finding of a normal blood amylase is a valuable means of excluding the pancreas as a cause of acute epigastric pain. Two such instances were recently observed by the author. In one, operation was performed and revealed an acutely inflamed appendix lying in the epigastrium attached to the falciform ligament. In the other, operation was not performed; coronary thrombosis was the final diagnosis, as revealed with the electrocardiogram and the subsequent clinical behavior of the patient.

SUMMARY.—(1) A number of patients were studied suffering from transient attacks of acute upper abdominal pain with nausea, vomiting and latent jaundice, in whom a clinical diagnosis of biliary colic, perforated ulcer, intestinal obstruction or coronary disease had been made.

(2) In each instance a very high concentration of blood amylase was found, when examined at the height of the attack, but which gradually returned to normal with the subsidence of symptoms.

(3) Anatomic evidence of disease of the pancreas was found in each instance coming to operation. The nature of the pancreatic lesion has been discussed.

REFERENCES

[1] Elman, R., Arneson, A. N., and Graham, E. A.: Value of Blood Amylase in the Diagnosis of Pancreatic Disease. Arch. Surg., **19**, 943, 1929.

[2] Elman, R.: Blood Amylase in Relation to Disease of the Pancreas: Further Observations. Arch. Int. Med., **48**, 828, 1931.

[3] Elman, R.: Acute Interstitial Pancreatitis. Surg., Gynec., and Obst., **57**, 291, 1933.

[4] Elman, R.: Acute Inflammation of the Pancreas. Surg., Gynec., and Obst., **61**, 670, 1935.

[5] Graham, E. A.: Acute Pancreatitis. Surg. Clinics N. Amer., **5**, 1387, 1925.

[6] Comfort, M. W.: Serum Lipase; Its Diagnostic Value. Proc. Staff Meetings Mayo Clinic, **10**, 810, 1935.

[7] Clasen, A. C., Johnstone, P. N., and Orr, T. G.: Blood Amylase in Experimental Pancreatitis. Surg., Gynec., and Obst., **59**, 756, 1934.

[8] McCaughan, J. M.: Value of Amylase of Blood, *etc.* Surg., Gynec., and Obst., **59**, 598, 1934.

THE VALUE OF PREOPERATIVE IRRADIATION IN TUMOR OF THE TESTIS

ALEXANDER RANDALL, M.D., AND ALBERT E. BOTHE, M.D.
PHILADELPHIA, PA.

WHENEVER there occurs, in the current medical literature, an unusual increase in the number of papers dealing with a given subject, one can feel measurably sure that either a new diagnostic method has been evolved, or that some new advance in therapy has become available; or perhaps someone has rudely awakened us to the realization of an unsuspected morbidity or, worse yet, mortality.

During the past 10 years 115 articles have appeared on the subject of testicular tumor, and two-thirds of these (76) have been published in the past five years. When we look for reasons, we find:

First: Tanner's report of 600 collected cases, nearly all treated by orchidectomy, 425 of which were followed, who states that after four years only 25 were well—cure, 5.3 per cent; mortality, 94.7 per cent. Hinman says, "Orchidectomy, even with early diagnosis, is a dismal failure"; and because of a mortality so appalling, he developed his radical operation, showing a definite, but hardly a satisfactory, improvement in the prognosis.

Second: The field of diagnosis has been greatly broadened and markedly improved since the demonstration of a gonadotrophic hormone in the urine when a tumor or its metastases are present in the body. With this there arrived not only an accuracy of diagnosis, but also a test that has been rapidly developed into an appreciable index of the type of malignant cell present, and its sensitivity to irradiation.

Third: There has come an advance in therapy by the addition of irradiation to surgery to such an extent that, as Keyes says, "Without irradiation prognosis is utterly bad."

We are anxious, therefore, to bring to your attention the evidence we have that makes us feel that irradiation should precede surgery, but that it should never supplant it entirely. This idea naturally followed the results obtained in kidney tumors in children, in which cases we pointed out the distinct advantage of preoperative irradiation. In testicular tumor the surgical procedure is rarely as difficult as in the case of renal neoplasm, but the clinicopathologic reasons remain the same.

Zondek, in 1929, first observed the appearance of a gonadotrophic hormone in the urine of a man suffering from a teratoma of the testis, and, three years later (1932), reported his observations on the use of this test in the diagnosis of teratomata in 14 cases. The test itself has been materially improved and refined, until today it stands, not only as a qualitative test, but as a quantitative one also. It is calculated in established mouse units the

---

Submitted for publication May 27, 1936.

titer of hormonal excretion, and this, in turn, can be applied as an index of both the type of tumor and its radiosensitivity. The feeling is growing that all testicular tumors are basically teratomatous in origin and that practically all exhibit some type of carcinomatous proliferation, while the characteristic round cell tumor, so frequently called a sarcoma in the past, is now the seminoma of Chevassu and arises from the adult germinal cells of the seminiferous tubules. One-sided overgrowth is the rule rather than the exception in all testicular tumors, so that frequently a tumor can be given rather definite characterizing features, though, as Ewing has pointed out, serial section of the whole tumor may be required to establish a positive opinion of a single cell type.

Ferguson has pointed out that the titer of the gonadotrophic hormone, Prolan A, is a rather specific index of the dominant type of tumor cell present, and that the mouse unit readings in the different groups overlap so little that it is possible to make a tentative diagnosis of the predominant cell type on this determination alone. The observation has also been made that, after irradiation of the primary tumor or its metastases, a prompt drop in the excretion titer of Prolan A in the urine is evidence of cell sensitivity, the rapidity, and extent of decrease, being excellent indices upon which to base a prognosis.

We have postulated the following acceptable facts to guide our surgery, bearing in mind that the clinical result is of greater interest than an academic discussion of tumor types:

First: The younger the cell, the greater its roentgen sensitivity.

Second: The younger the dominant cell type, the more frequent and the earlier the metastases.

Third: In the face of existent metastases, irradiation should, of course, precede the orchidectomy.

Fourth: If this last be true in gross visible metastases, it should be even more essential if metastatic involvement is just beginning.

Based on these assumptions, therefore, it has been our practice for the past three years to:

First: Have a Wassermann and a Prolan A determination.

Second: Begin immediately the administration of deep roentgen therapy.

Third: Perform an orchidectomy at any interval up to five weeks after the last roentgen ray treatment.

In considering the preoperative roentgen therapy, Doctor Pendergrass has felt that too heavy irradiation over the primary tumor may be actually traumatic and provocative of cell dispersion, just as one may traumatize a lesion in performing a biopsy. He has obtained the impression that in epidermoid carcinoma of the lip a violent local reaction is apt to occasion an adenopathy in excess of a simple reactionary lymphangiitis; in fact, some of these nodes have been proven to be malignant, and these observations have been made in patients who did not have palpable nodes prior to irradiation. The approach, therefore, is from the periphery, converging toward the focus of the disease, and in testicular tumor irradiation includes the lymphatic channels from the chin to the tuber ischii anteriorly and posteriorly; it being hoped, thereby, to destroy metastatic foci of any size, to create a field resistant to malignant cell implantation, and, finally, to administer daily to the immediate lymph drainage radicals and the local tumor, a small, protracted dose, up to the limit of skin tolerance, keeping in mind the general resistance of the patient, as determined by biweekly blood counts.

Pathologic Considerations.—The mixed tumors of the testicle can be divided into three groups, when they are studied relative to their degree of radiosensitivity.

Group I.—*The tumors that are made up of undifferentiated anaplastic immature cells.* In this group, two different types have been observed. One type is made up almost entirely of small round embryonal cells with very little cytoplasm (lymphoid). In the other the predominating cell is somewhat larger but definitely anaplastic (seminoma). The stroma is scant in both, and the vascularity is abundant with vessels in different stages of development.

Group II.—*In this group may be placed the adult teratomata.* The epithelial cells are large, well developed, and differentiation is evidenced throughout the tumor. They are in tubular or acinar arrangement. Occasionally small areas of imperfectly differentiated cells are seen. The vascularity is variable. In some fields the vessel development is hemangiomatous. Cartilage, bone and calcium are not infrequently seen. Dense whorls of fibrous tissue and myxomatous degeneration are usually present.

Group III.— *This group, like Group II, is very complex, but differs from the previous group by showing a greater diversity in the stages of cellular development.* These tumors are made up partially of anaplastic and partially of well differentiated cells. In some the embryonal elements predominate; in others the adult teratomatous structures predominate. The microscopic findings in this group are characteristic of radiosensitivity and radioresistance. The degree of regression from irradiation must apparently be dependent upon the number of anaplastic cells.

The gross changes encountered in these tumors after irradiation ranged from little or no regression to a dramatic disappearance of any palpable neoplasm (Fig. 1). In attempting to evaluate the microscopic changes after irradiation, these have been divided into three groups: first, those which have undergone complete regression; second, those upon which irradiation has had no apparent effect; and finally, those which have undergone partial regression.

The histologic findings in the tumors which have undergone complete regression present two totally different pictures. In one the tumor was made up of closely packed shadow cells. They stained a very light pink with hematoxin and eosin. They are imperfectly outlined with the nucleus and cytoplasm undifferentiated. The form of the shadow cells which predominate in the tumor is not unlike those seen in the nonirradiated seminoma. Scattered in the meshes of these necrotic cell forms an occasional single deeply staining small round cell is seen. These appear as active, viable cells which have not been destroyed by irradiation (Fig. 2). The blood vessel changes consist of endarteritis of the small vessels but no evidence of complete obliteration. There is no increase in the connective tissue. In general, the appearance is that of necrotic cells without displacement fibrosis. If the surgical removal had been effected a week later, the tissue would have appeared as though it had undergone cystic necrosis.

In the other type with complete regression, the tumor is represented by displacement fibrosis with hyalinization and remnants of seminiferous tubules. The blood vessels give definite evidence of endarteritis with occasional obliteration. There are no cells, or remnants of cells, to permit identification or even speculation as to the cell of origin (Fig. 3). When the sections are compared with those made from irradiated mixed tumors of the kidney, they are identical with the displacement fibrosis which displaces the small round celled sarcomatous areas.

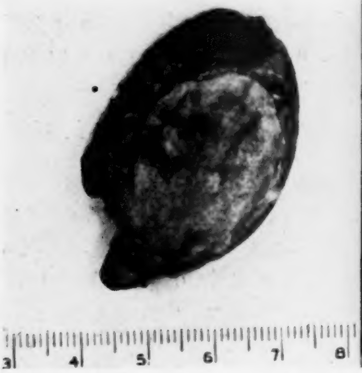

Fig. 1.—Tumor of the testis after regression from irradiation. This tumor before irradiation was the size of an orange. It was not palpable after irradiation.

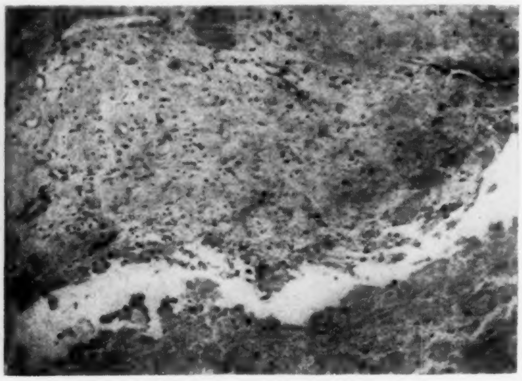

Fig. 2.—Photomicrograph of a section of the tumor shown in Fig. 1. This illustrates the shadow cell type. Small black dots represent remaining viable cells.

In the second group are those upon which irradiation had no apparent effect. The microscopic picture is very complex and varied. The epithelial cells of different types are differentiated. The fibrous connective tissue is the mature adult type. In general, the picture is not unlike that described in Group II of the nonirradiated tumors (Fig. 4).

In the third group, those which have undergone partial regression, the findings are somewhat variable. Epithelial cells in different stages of development and differentiation are frequently seen. Areas with extensive fibrous changes with collections of shadow cells are evident in scattered fields. The blood vessels in some places show endarteritis while in others they are unchanged. The tumors in this group before irradiation were made up of cells ranging from immature anaplastic lymphoid and epithelial types to the adult well differentiated cell. The former were destroyed, and are represented by shadow cells and fibrosis. The latter, due to their resistance, were not appreciably affected by the irradiation (Fig. 5).

In general, the irradiation of testicular tumors has a definite destructive effect upon the immature embryonal cells, but little or no effect upon the differentiated types. These observations are in keeping with the laws governing cellular radiosensitivity.

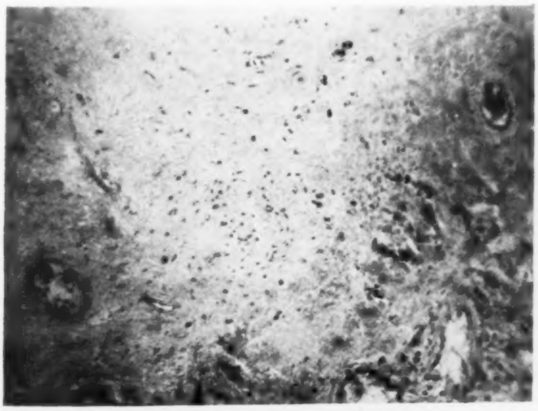

FIG. 3.—Photomicrograph of a section of a tumor of the testis, with complete regression from irradiation. This illustrates the replacement by fibrous tissue.

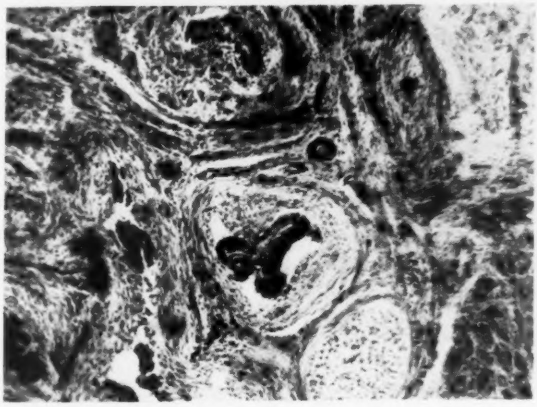

FIG. 4.—Photomicrograph of a section of an adult teratoma type of tumor of the testis. There is no evidence of regression from irradiation.

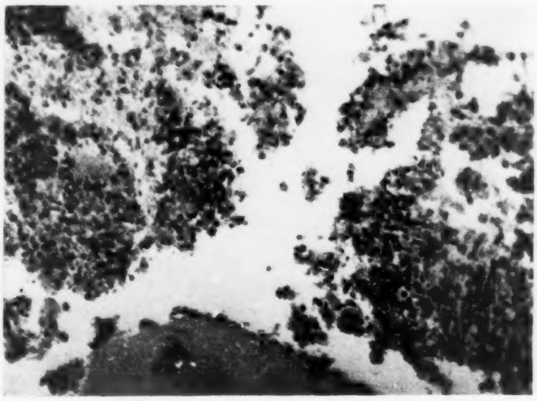

FIG. 5.—Photomicrograph of a section of a tumor of the testis, with partial regression from irradiation. This shows large islands of viable cells that have not been destroyed by irradiation.

In view of the foregoing observations it is very evident that, regardless of the degree of clinical improvement, irradiation does not entirely destroy the neoplasm. In that class in which there were occasional viable cells remaining which appeared to have the power of regeneration, it is felt that these tumors should be removed surgically, after the maximum regression from irradiation has been obtained. Procrastination after effective irradiation leads to disaster. The most favorable time for removal is usually between the fifth and sixth week.

CONCLUSIONS

We have attempted to demonstrate, both from clinical reasoning and from cellular pathology, the advantages to be gained by preoperative irradiation in tumor of the tesis. Certain points are outstanding and bear accentuation:

(1) That orchidectomy alone has given less than 10 per cent of cures; that radical surgery by orchidectomy, with the removal of the entire lymph drainage area, has raised this figure to 19 per cent cured; and that irradiation alone has produced 29 per cent of cures.

(2) That if irradiation is to be considered of benefit, its greatest clinical value is to be obtained by its use preoperatively. We have presented and discussed the cellular reactions as observed in both irradiated and unirradiated tumors, and find the results in keeping with the laws governing cellular radiosensitivity.

(3) That irradiation alone cannot be relied upon to produce a cure because of resistant cells; nor can a cure be appreciated, measured or established by any clinical test. Therefore, orchidectomy is mandatory as a secondary procedure.

(4) That irradiation should be widespread in its application, and should include the entire body above the primary lesion.

It is our conviction that the proper application of these principles will raise the percentage of cures in tumors of the testis well above those at present obtained.

DISCUSSION.—DR. FRANK E. ADAIR (New York) stated that there is no phase of modern medicine which so strikingly demonstrates the advance made along the lines of both diagnosis and exact therapy, than in the case of teratoma of the testis, the diagnosis and therapy of which have always been difficult and inexact. A few years ago, a new diagnostic aid was given us in the form of a "therapeutic radiation test." Up until this time the diagnosis was based upon a consideration of (1) the findings by palpation which revealed the consistency and the anatomic boundaries of the enlargement; (2) the transillumination test; and (3) the result of the Wassermann test.

Now, a most valuable diagnostic addition is given us in the form of a hormone reaction. By testing the presence of the Prolan A in amounts above 100 mouse units, we must suspect the presence of a teratoma of the testis if over this amount is found. This interesting test goes farther and gives us an idea of the exact histopathology of the tumor. The Prolan A test becomes a valuable aid in the periodic follow up of the case. It is an easy matter to test the urine of the patient for the presence of excessive amounts of Prolan A. It is a sign of the presence of recurrence or metastasis, far more delicate, and more reliable than any clinical or roentgenologic examination.

The next great advance in this disease was given by radiation therapy. We are all familiar with the disappointing accomplishments of surgery alone, in this, one of the most malignant of all human tumors. Wasterlain's studies show only 6 per cent of five year cures by orchidectomy alone. Hinman revived the operation of Chevassu, which is one having a high mortality (12.2 per cent), and found but 17 per cent free of disease at the end of five years. Barringer and Dean, of the Memorial Hospital, reported their cases in 1928, and found that by using radiation therapy they had 29.2 per cent free of disease at the end of five years. This encouraging figure was accomplished in spite of the remarkable fact that 89 per cent of the 154 cases reported were inoperable on admission. The greatly increased percentage of cures was obtained by employing the roentgen therapy technic available at that time. Since then, Coutard has developed the fractional dose method of applying radiation which has the double advantage of being able to give larger doses to the tumor and metastatic deposits; and, furthermore, the tolerance of the patient to the treatment is much greater.

To properly treat this disease the radiologist must have a good understanding of its anatomy. Frequently the first complaint of the patient is that of indigestion or a pain in the back. The disease invades the lymphatics and the veins and appears not only in the groin but also at the celiac axis and mediastinum.

At present our treatment consists in preliminary radiation of the testis and surrounding areas including the lower quadrants of the abdomen, the suprapubic area and the inguinal nodes. Approximately six weeks later orchidectomy is performed. Following the operation, the patient is irradiated by the divided dose technic, from the level of the diaphragm down to the trochanters, both anteriorly and posteriorly.

We have divided our teratomata of the testis into five groups:

(1) The adult type—those possessing cartilage, lung tissue, *etc.* The incidence is about 10 per cent.

(2) The seminoma—the large cell type. Incidence, 16 per cent.

(3) The embryonal carcinoma with the lymphoid stroma; very radiosensitive. Incidence, 40 per cent.

(4) Embryonal adenocarcinoma. Incidence, 33 per cent.

(5) Chorio-epithelioma. Incidence, 1 per cent.

There is no doubt in my mind but that this newer principle of radiation will add materially to the present five year cure rate of 29.2 per cent. In fact, Ferguson, of our clinic, has already utilized this newer technic, and has obtained freedom from disease in a three year period, of 52.6 per cent.

SHOCK SYNDROME FOLLOWING SUBCUTANEOUS INJECTION OF BILE OR BILE SALTS

Edmund Andrews, M.D., Henry N. Harkins, M.D., Ph.D., Paul H. Harmon, M.D., Ph.D., and Jeanne Hudson, B.S.

Chicago, Ill.

FROM THE DOUGLAS SMITH FOUNDATION AND THE SERVICE OF DR. EDMUND ANDREWS, DEPARTMENT OF SURGERY, THE UNIVERSITY OF CHICAGO

In previous publications,[1, 2] the writers demonstrated that changes similar to those found in so called secondary shock were found in experimental peritonitis due to bile or bile salts. These changes included a marked fall in blood pressure, a definite hemoconcentration and a reduction in bleeding volume associated with a marked effusion of plasma like exudate into the peritoneal cavity. This fluid loss was considered to be an important lethal factor in the experiments in question, especially since, in many instances, these animals died without evidences of anaerobic infection. On the other hand, the work of Andrews, Rewbridge and Hrdina[3] indicated that death, after the subscapular injection of bile salts, resulted from infection by anaerobic organisms. This apparent difference in the action of bile or bile salts when injected subcutaneously, intramuscularly, or intraperitoneally prompted the present experiments.

Andrews, Thomas and Schlegel[4] found that pieces of liver inserted into the axilla produced death, which was thought to be the result of toxemia. Horrall and Carlson[5] and Horrall[6] found that subcutaneous injection of bile in ten dogs caused more variable results than the intraperitoneal injection. Dogs receiving more than 4 cc. per Kg. died within 24 hours and some of the dogs receiving as low as 2 cc. per Kg. died within the same time. There was excessive edema at the site of injection. Dogs receiving less than 2 cc. per Kg. developed large necrotic sloughs at the site of injection, but usually did not die. Andrews, Rewbridge and Hrdina[3] reported that after injections of sterile 10 per cent bile salt solution or of liver extract under the scapulae of dogs, there resulted in most cases an obvious gas gangrene with positive cultures for anaerobic organisms. In a later paper[7] these authors give protocols of eight experiments in which 10 per cent bile salt solution was injected subcutaneously. All these dogs died within 24 hours, and of six in which cultures were made, all showed Cl. welchii and the site of injection showed gas and induration.

Experimental Investigation.—Group I: Eight dogs were anesthetized with morphine and ether during the time of injection. The animals were marked along the midline of the dorsal and ventral surfaces and the injections made subcutaneously into the axilla and groin of one side (the right in five animals, the left in three animals). Two animals received 10 cc. of sterile dog gallbladder bile per Kg. and the other six received 10 cc. of sterile 10 per cent repurified Armour's bile salt solution. Hemoglobin determinations were

---

Submitted for publication June 30, 1936.

made by the Sahli method and with the Van Allen hematocrit, the readings being made before injection and at intervals thereafter until death. All the animals died in from seven to 34 hours, the average being 21 hours. Cultures of the subcutaneous tissues at the site of injection were then taken after iodine sterilization of the overlying skin and incision with a red hot knife. Anaerobic cultures were taken using both swab and tissue block technic. The animals were then bisected in a manner previously described,[8] and the contralateral halves weighed. The organs were then examined grossly and microscopically. Chemical analyses of the fluid exuded into the tissues at the site of injection were made in three instances by a previously described method.[3]

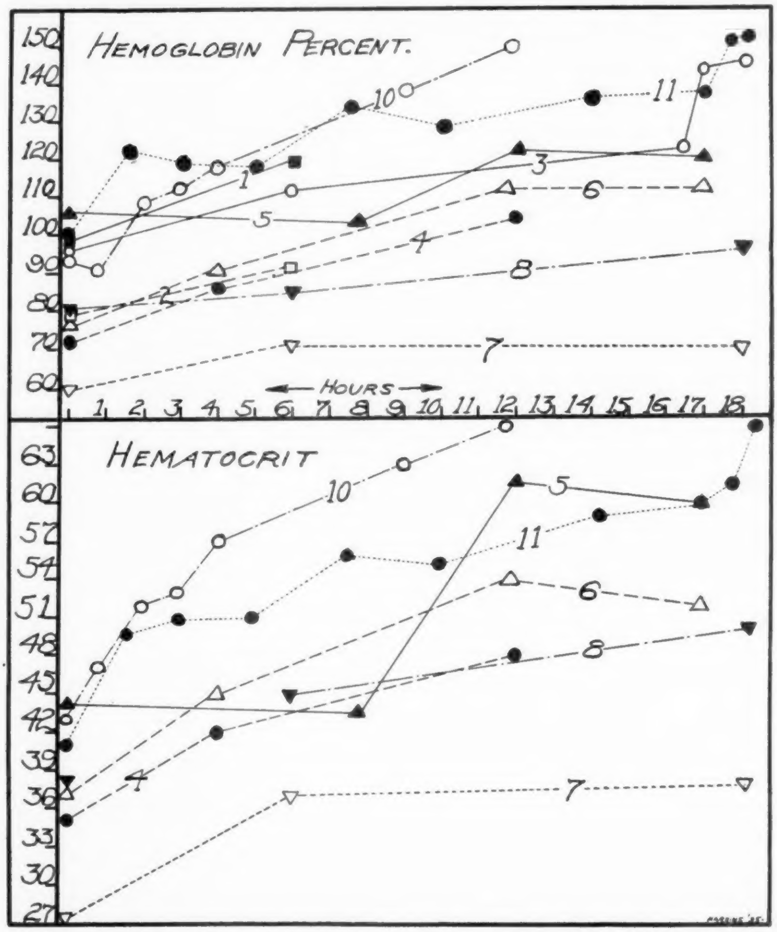

CHART 1.—Shows the rise in hemoglobin percentages and hematocrit readings following subcutaneous bile and bile salt injections. The final hemoglobin reading of 53 per cent obtained 29 hours after the injection of bile in Experiment 7 is not included in the chart. The last two values in Experiment 3 were obtained 23 and 28 hours after the injection of bile salts, but are shown in the chart. Similarly the last two results shown at the right in Experiment 11 were obtained 20 and 22 hours respectively after the injection of bile salts.

Group II: Three dogs were thoroughly anesthetized with sodium barbital (250 mg. per Kg. body weight, intraperitoneally) and were then placed on a tipping apparatus previously described,[8] after the application of a body case. This apparatus consists of a balanced tray with a connection to a recording marker on a kymographic drum, so that any tipping of the animal to one side or the other can be registered. After a control tracing, the apparatus was steadied and 10 cc. of 10 per cent bile salt solution were injected subcutaneously into the axilla and groin on one side. The kymograph tracing then recorded the immediate shift in weight to the injected side due to the weight of the fluid injected and any later shift until the time of death. One of the three animals received an injection on one side of normal saline solution equal in amount to the volume of bile injected on the opposite side, so that there was no immediate shift of weight. In this same experiment there was a continuous recording of the blood pressure until death. This was done by inserting the usual carotid arterial cannula and connecting it with the recording manometer by means of a flexible rubber tube so that interference with the tipping of the apparatus was reduced to a minimum. The cannula was fastened to the midline of the animal so that tipping of the apparatus would not affect the blood pressure base line. Frequent hemoglobin and hematocrit readings were made. At necropsy no cultures or chemical examinations of the fluid forming the local edema were made of these three animals. Bisection and necropsy were performed, however. As a control of the determination made by the bisection method, the difference in weight was observed by counterbalancing the tipping apparatus,[8] only the counterbalancing weights were placed 12 cm. from the midline of the apparatus, as this seemed to correspond to the average distance of the center of the edematous area from the midline.

RESULTS.—The animals all died within 34 hours and all showed a rise in hemoglobin and hematocrit (Chart 1). All animals showed a marked excess in weight of the injected side. This difference in weight in the eight experiments in Group I averaged 3.5 per cent of the body weight (Table I). The three additional animals placed on the tipping apparatus showed a corrected

TABLE I

THE EFFECT OF INJECTION OF BILE SALTS AND WHOLE BILE SUBCUTANEOUSLY

Experiment	1	2	3	4	5	6	7	8	Average
Dog wgt. Kg.	8.0	6.0	6.0	8.0	13.0	8.0	5.6	5.2	7.5
Sex	M	F	F	M	M	M	F	F	..
Cc. bladder bile	..	..	..	..	..	..	56	52	..
Cc. 10 per cent bile salt sol.	80	60	60	80	130	80	..	..	..
Hours before death	16	7–17	28–34	15	20	20	29	19–29	21
Increase Hb. per cent	21	11	50	33	16	36	12	17	25
Increase hematocrit	..	..	..	13	18	17	10	12	14
Wgt. injected side*	2,645	1,995	1,817	2,795	4,695	2,685	1,780	1,605	..
Wgt. normal side	2,195	1,775	1,557	2,500	4,230	2,285	1,440	1,390	..
Wgt. difference Gm.	450	220	260	295	465	400	340	215	..
Corrected difference	370	160	200	215	335	320	284	163	..
Per cent body weight	4.6	2.7	3.3	2.7	2.6	4.0	5.1	3.1	3.5

*The weights of the two sides of the animal were determined by Blalock's bisection method. In three experiments (2, 3, and 8) death of the animal occurred some time during the interval listed. In computing the average number of hours before death, the median time is used in these instances.

excess in weight of the injected side of 3.9, 3.8 and 3.9 per cent body weight. The average for the whole series of 11 animals is 3.6 per cent body weight.

Bacteriologic.—Cultures were made of the edematous tissue at the site of injection in the first eight experiments. In Experiments 4, 5 and 6 these cultures were taken one hour, five minutes and two minutes after death, respectively, and there was no growth. The culture from Experiment 1, taken one hour after death, grew only Staphylococcus albus (possibly a contaminant). On the other hand, in Experiments 2, 3, 7 and 8, cultures taken seven hours, three and one-half hours, five minutes, and six hours respectively after death showed no aerobic growth, but in all four instances a large gram-positive anaerobic bacillus grew in the anaerobic media. Since, in all instances, both edematous subcutaneous tissue and muscle were cultured, the organisms found here may be similar to those found by other authors in normal dog muscle.[7] At least, their presence in our experiments was not constant, being found in only one-half of the eight experiments. All but one of these positive results were cultured more than three hours after death. It is quite possible, therefore, that postmortem contamination may account for some of the organisms found. Although at least one-half of the animals died without cultural evidence of anaerobic organisms, all had the fluid shift previously described.

Pathologic.—Necropsy examination revealed moderate hemorrhage in the adrenal glands especially in the reticular zone and hemorrhage in the mesenteric nodes. There was some blood staining of the bowel contents in two instances, but no petechial hemorrhages in the bowel wall. The most marked change, however, was the extensive edema of the subcutaneous tissue at the site of injection. Sections of the skin, subcutaneous tissue and muscle near the injection were taken in Experiments 9 and 10 and showed extensive edema. Some of the muscle bundles and fibrous tissue showed lack of normal staining reaction with karyorrhexis of the nuclei. In Experiment 10 there were several collections of polymorphoneuclear neutrophiles. Some of the individual muscle fibers were separated from each other by edema and some of the capillaries were engorged with blood.

Chemical.—The most striking item of the analysis of the exuded fluid was

TABLE II

CHEMICAL ANALYSIS OF FLUID IN EDEMATOUS TISSUE, PRODUCED BY THE SUBCUTANEOUS INJECTION OF STERILE 10 PER CENT BILE SALT SOLUTION*

Experiment	NaCl Mg./100 cc.	NPN Mg./100 cc.	Sugar Mg./100 cc.	Total Protein Gm./100 cc.
4 Fluid	598	120	0	3.5
5 Fluid	570	125	163	4.6
6 Fluid	593	160	108	4.6
Control Plasma	582	36	109	5.0
Control Plasma	610	29	109	6.2

*Figures for two normal dogs' blood plasma analyses are given. It is seen that the fluid in the edematous tissue and normal blood plasma are essentially similar except that the nonprotein nitrogen content of the fluid is greater and the total protein content is slightly less.

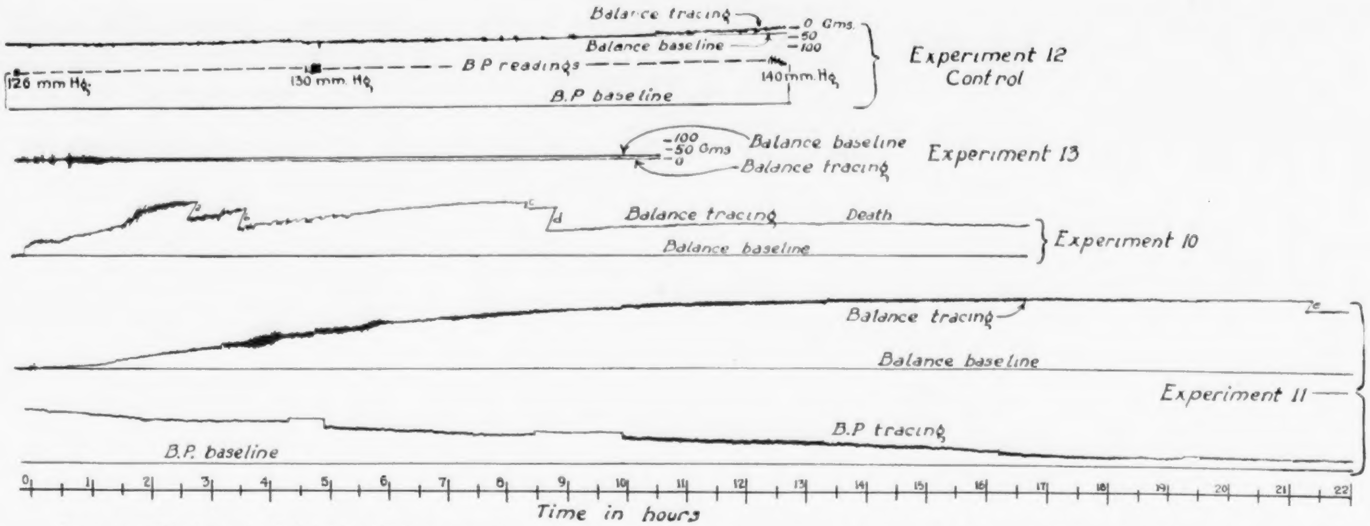

CHART 2.—Tipping of a balanced animal to the side of injection following subcutaneous injection of bile salts. This chart is a composite record of four experiments. In Experiment 12 there are a control balance tracing and control blood pressure tracing. It is seen that there is practically no tipping of the animal even after 14 hours, and that the blood pressure remained constant during this interval. Control hemoglobin and hematocrit readings were 106 and 53; at the end of five hours they were respectively 112 and 50, and at the end of 14 hours were 105 and 51. At the right hand end of the balance tracing the sensitivity of the balance is determined by the counterbalance method with the weights 12 cm. from the midline. It is seen that the total shift had amounted to less than 50 Gm. The biscetion method gave a difference in weight between the two sides of the animal of 45 Gm. (Dog weight = 6.0 Kg.). In Experiment 13 a control balance tracing is shown. The amount of shift at the end of 11 hours is shown by the counterbalance method to be less than 50 Gm. In Experiment 10 a balance tracing after injection is shown. At the zero hour mark 10 cc. of a 10 per cent of bile salt solution were injected into the right axilla and groin with a resultant immediate shift to the injected side because of the weight of the injected solution. The following gradual fluid shift was so marked at points *a*, *b*, *c*, and *d*, that counterbalancing weights of 100, 100, 50, and 100 Gm. were added 12 cm. to the left of the midline of the balance. In Experiment 11 a balance tracing and associated blood pressure tracing are shown. At the zero hour mark 10 cc. 10 per cent bile salt solution were injected into the right axilla and groin and simultaneously a similar amount of normal saline solution into the left side; so that there is no immediate fluid shift. The gradual fluid shift became so marked at point *c* that a counterbalance weight of 100 Gm. was added 12 cm. to the left of the midline of the balance.

that its total protein content averaged about 80 per cent of that of normal blood plasma; that found after burns or freezing is similarly slightly less concentrated than blood plasma in total protein content. The increase in the nonprotein nitrogen content may be in part due to contamination with bile salts.[2] The sodium chloride content was essentially similar to that of blood plasma (Table II).

The three animals that were placed on the tipping apparatus all showed a steady tipping toward the injected side. This tipping seemed to show a relation to the hemoconcentration as represented by the increase in hemoglobin percentage and in the hematocrit readings. In the one experiment in which the blood pressure was measured the tipping and blood pressure fall were somewhat proportionate as seen in Chart 2. Protocols of the three tipping experiments follow:

Experiment 9.—Dog weight 5.4 Kg., 260 mg. sodium barbital per Kg. Injection of 60 cc. of 10 per cent bile salt solution subcutaneously in right groin and right axilla at 2:40 P. M. Gradual tipping of apparatus in form of decelerating curve until death at about midnight (approximately nine hours after injection). No blood counts. Counterbalance difference in weight of two sides = 200 Gm. Weight right side bisected animal = 1,780 Gm., left side = 1,510 Gm., difference = 270 Gm., or 5.0 per cent body weight by bisection method. This amounts to 3.9 per cent body weight when corrected for the amount of solution injected. Since some of the bile salt solution is probably absorbed, the true value lies somewhere between the weighed and corrected values. Necropsy negative except for bloody fluid in small bowel, an enlarged thyroid gland and extensive edema at the site of injections.

Experiment 10.—Dog weight 8 Kg., female, 250 mg. sodium barbital per Kg. Injection of 80 cc. of 10 per cent bile salt solution in right groin and right axilla 2:20 P. M. Gradual tipping in form of decelerating curve until death at 4:20 A. M. (14 hours after injection) (Table III).

TABLE III

Time	Hemoglobin Per Cent	Hematocrit
Control	93	43
2:20 P.M.	injection	..
3:00 P.M.	91	47
4:00 P.M.	109	52
5:10 P.M.	112	53
6:30 P.M.	118	57
11:00 P.M.	138	63
1:40 A.M.	150	66
4:20 A.M.	death	..

Counterbalance difference in weight of two sides = 360 Gm. Weight right side bisected animal = 2,670 Gm., left side = 2,290, difference = 380 Gm., or 4.8 per cent body weight by bisection method. When corrected for weight of solution injected = 3.8 per cent body weight. Necropsy negative except for slight medullary hemorrhage in both adrenal glands and extensive edema at site of injections.

Experiment 11.—Dog weight 7 Kg., female, 260 mg. sodium barbital per Kg. Injection of 70 cc. of 10 per cent bile salt solution in right groin and right axilla and 70 cc. normal salt solution into left groin and left axilla at 12:30 P. M. Gradual tipping in form of decelerating curve until death at 12:00 noon next day (23½ hours after injection). Simultaneous blood pressure tracing; no immediate effect from injection; gradual fall to 28 Mm. Hg. three minutes before death.

TABLE IV

Time	Hemoglobin Per Cent	Hematocrit	Blood Pressure
Control	101	41	170 Mm. Hg.
12:30 P.M.	injection	..	...
2:00 P.M.	122	50	155 Mm. Hg.
3:45 P.M.	118	51	128 Mm. Hg.
5:20 P.M.	118	51	115 Mm. Hg.
8:00 P.M.	133	56	95 Mm. Hg.
10:30 P.M.	129	55	87 Mm. Hg.
2:10 A.M.	136	59	74 Mm. Hg.
5:10 A.M.	138	60	55 Mm. Hg.
8:00 A.M.	151	61	40 Mm. Hg.
10:35 A.M.	152	66	34 Mm. Hg.
12:00 M.	death	..	..

Counterbalance difference in weight of two sides = 530 Gm. Weight right side bisected animal = 2,250 Gm., left side = 1,975 Gm., difference = 275 Gm. or 39 per cent body weight by bisection method. No correction is applied because of the saline injection on the opposite side. Necropsy negative except for extensive edema at site of injections.

Control experiments on the changes in blood pressure and blood concentration are detailed by Harkins.[9] Two control experiments are shown in Chart 2. In these experiments, animals anesthetized with barbital were placed on the tipping apparatus. Simultaneous blood pressure readings in Experiment 12 showed no decrease. In neither of the two experiments was there an appreciable tipping of the apparatus.

COMMENT.—Previous workers[1, 2, 8, 9, 10 to 18] have shown that the loss of whole blood or blood plasma amounting to more than 3 per cent body weight into the tissues or externally, as in hemorrhage, is apt to cause death. Such a loss represents almost 50 per cent of the blood volume (calculated as one-thirteenth of the body weight) and corresponds to a hemorrhage of over two liters in a 70 Kg. man. To be of serious import such a loss must occur in a relatively short time. In Blalock's work[11] on burns the animals lost an average of 3.3 per cent body weight of plasma into the tissues after an average of 15 hours. In the present series of 11 animals the average loss of similar fluid was 3.5 per cent body weight after an average of 19 hours.

The question as to whether the loss of plasma or blood as found in various types of shock by previous workers is sufficient to cause death, or even be a major factor in the death of the experimental animals in question, is not within the province of this paper. However, if it is assumed that the physical explanation of shock applies to burns, freezing, intestinal trauma, trauma to an extremity, and simple hemorrhage, then it can equally well be applied to the effects of subcutaneous bile or bile salt injection.

Since the subcutaneous injection of bile or bile salts produces an exudation of plasma like fluid similar to that found intraperitoneally in bile peritonitis, the present experiments demonstrate that there is no qualitative difference in the action of bile depending on the site of action. This refutes one possible objection to the theory that secondary surgical shock is one of the chief lethal factors in bile peritonitis. The action of the bile or bile salts when injected subcutaneously or intraperitioneally is probably that of a local irritant. Anesthesia had to be particularly deep during the time of injection to prevent all evidences of pain. The biliary solutions probably injure the capillaries at the site of injection with a resultant local leakage of protein containing fluid.

CONCLUSIONS

(1) The subcutaneous injection of bile or bile salts causes a local exudation of plasma like fluid into the tissues. This fluid amounted in 11 experiments to an average of 3.8 per cent body weight with death 19 hours after injection. There was an accompanying hemoconcentration and blood pressure fall.

(2) This fluid exudation is sufficient in quantity to be a lethal factor of importance.

(3) The parallelism of the action of bile or bile salts when injected subcutaneously and intraperitoneally in producing a shock like syndrome affords reciprocal evidence for the importance of secondary surgical shock as a lethal factor in the two conditions.

REFERENCES

[1] Harkins, H. N., Harmon, P. H., Hudson, J., and Andrews, E.: Mechanism of Death in Bile Peritonitis. Proc. Soc. Exper. Biol. & Med., **32,** 691, 1935.

[2] Harkins, H. N., Harmon, P. H., and Hudson, J.: Lethal Factors in Bile Peritonitis: I. Surgical Shock. Arch. Surg. **33.** 576, 1936.

[3] Andrews, E., Rewbridge, A. G., and Hrdina, L.: Causation of B. Welchii Infection in Dogs with Sterile Liver Extract and Bile Salts. Proc. Soc. Exper. Biol. & Med., **28,** 136, 1930.

[4] Andrews, E., Thomas, W. A., and Schlegel, K.: Newer Aspects of Liver Disease. Surg., Gynec. & Obstet., **47,** 179, 1928.

[5] Horrall, O. H., and Carlson, A. J.: The Toxic Factor in Bile. Am. J. Physiol., **85,** 591, 1928.

[6] Horrall O. H.: The Toxicity of Bile. Univ. of Chicago Science Series, **6,** 287, 1927–1928.

[7] Andrews, E., Rewbridge, A. G., and Hrdina, L.: Causation of Bacillus Welchii Infections in Dogs by Injection of Sterile Liver Extracts or Bile Salts. Surg., Gynec. & Obstet., **53,** 176, 1931.

[8] Harkins, Henry N.: Shift of Body Fluids in Severe Burns. Proc. Soc. Exper. Biol. & Med., **31,** 994, 1934. Experimental Burns. I. The Rate of Fluid Shift and Its Relation to the Onset of Shock in Severe Burns. Arch. Surg., **31,** 71, 1935.

[9] Harkins, H. N.: The Bleeding Volume in Severe Burns. ANNALS OF SURGERY, **102,** 444, 1935.

[10] Parsons, Eloise, and Phemister, D. B.: Hemorrhage and Shock in Traumatized Limbs. Surg., Gynec. & Obstet., **51,** 196, 1930.

[11] Blalock, Alfred: Experimental Shock. VIII. The Importance of the Local Loss of Fluid in the Production of the Low Blood Pressure after Burns. Arch. Surg., **22,** 610, 1931.

[12] Blalock, Alfred: Experimental Shock: The Cause of the Low Blood Pressure Produced by Muscle Injury. Arch. Surg., **20,** 959, 1930.

[13] Underhill, Frank P., Kapsinow, Robert, and Fisk, Merl E.: Studies on the Mechanism of Water Exchange in the Animal Organism. I. The Nature and Effects of Superficial Burns. Am. J. Physiol., **95,** 302, 1930.

[14] Domenech-Alsina F., Benaiges, B., Arqué, P.: Etude du choc provoqué par l'irrigation péritonéale hypertonique. Compt. rend. Soc. de biol., **114,** 104, 1933.

[15] Scott, H. G., and Wangensteen, O. H.: Blood Losses in Experimental Intestinal Strangulations and Their Relationship to Degree of Shock and Death. Proc. Soc. Exper. Biol. & Med., **29,** 748, 1932.

[16] Elman, Robert, and Cole, Warren H.: Hemorrhage and Shock as Causes of Death Following Acute Portal Obstruction. Arch. Surg. **28,** 1166, 1934.

[17] Roome, N. W., Keith, W. S., and Phemister, D. B.: Experimental Shock: The Effect of Bleeding after Reduction of the Blood Pressure by Various Methods. Surg., Gynec. & Obstet., **56,** 161, 1933.

[18] Harkins H. N.: Shock Due to Freezing: I. Shift of Body Fluids and Associated Blood Concentration Changes. Proc. Soc. Exper. Biol. & Med., **32,** 432, 1934; Harkins, H. N., and Hudson, J. E.: Shock Due to Freezing: II. Composition of Edema Fluid, *Ibid.*, 434; Harkins, H. N., and Harmon, P. H.: Experimental Freezing: Bleeding Volume, General and Local Temperature Changes, *Ibid.*, 1142, 1935.

SPINAL EXTRADURAL CYSTS

RALPH B. CLOWARD, M.D.
CHICAGO, ILL.

FROM THE DIVISION OF NEUROLOGY AND NEUROSURGERY, UNIVERSITY OF CHICAGO CLINICS, CHICAGO, ILL.

EXTRADURAL cysts in the spinal canal which are neither parasitic nor dermoid in origin are rare. Elsberg, Dyke and Brewer,[1] in 1933, reported four cases of extradural cysts which they found in their records among some 250 cases of tumors within the spinal canal. The believed their cases to be the first of this kind to be published. Lehman,[2] in 1935, however, found three previously reported cases, and added two very interesting cases of his own.

Case Report.—E. S., No. 125153, a white male, age 43, entered the University of Chicago Clinics April 2, 1935, complaining of increasing weakness, weariness and heaviness of both legs and lower part of his back for the past two years, marked chronic constipation for one year, and difficulty in starting the urinary stream for the past few weeks. He had been quite well until 1932 when the right foot and ankle became stiff and soon afterward he noticed the same thing on the left side. He found that after walking a short distance his feet and ankles would become weak and would not support him. This increased until he could walk only a block at a time. He also observed that the weakness was traveling up the legs involving the thigh muscles. In October, 1934, he began having pains, for the first time, in his thighs and hips. The strength of the legs had so markedly diminished that the patient could walk only a few steps. He had noticed muscular twitchings in his thighs and was conscious that the sensation in his legs was not the same as in his arms. The symptoms were much more severe in the right leg. The patient's past history was essentially negative. He had had no serious illnesses, operations or accidents. Other than the above complaints he was in good health.

Examination.—The general physical examination was negative except for some badly decayed teeth. The cranial nerves and upper extremities were essentially normal. There was loss of cutaneous sensation over the area of the twelfth thoracic dermatome with reduction to pin prick, light touch and temperature over the area of L_I. In both lower extremities below this level there was a less marked reduction of cutaneous sensation to all stimuli. Response to stimuli was more readily elicited on the left than the right lower extremity. There was complete loss of the sense of position and vibration from the iliac crests down. The sensation of deep pain was grossly reduced in both Achilles tendons. There was definite atrophy in the quadriceps muscles with muscular fibrillation in both anterior and posterior groups of thigh muscles. The knee and ankle jerks were active, especially on the right. There was a sustained ankle clonus with a marked extensor plantar reflex on the right, but none on the left. The Romberg sign was positive and coordination was poor. A tentative diagnosis of a spinal cord tumor was made with the upper level at D_{XII}, and spinal puncture and roentgenologic examination of the spine were advised.

The spinal fluid showed an initial pressure of 120. The fluid level in the manometer rose and fell rapidly upon making right and left jugular and abdominal pressure, respectively. It was colorless and contained no cells, showed no increase in protein, and the Wassermann test was negative. The findings of a normal cerebrospinal fluid and absence of obstruction of the spinal canal were rather surprising in view of the clinical

---

Submitted for publication July 23, 1936.

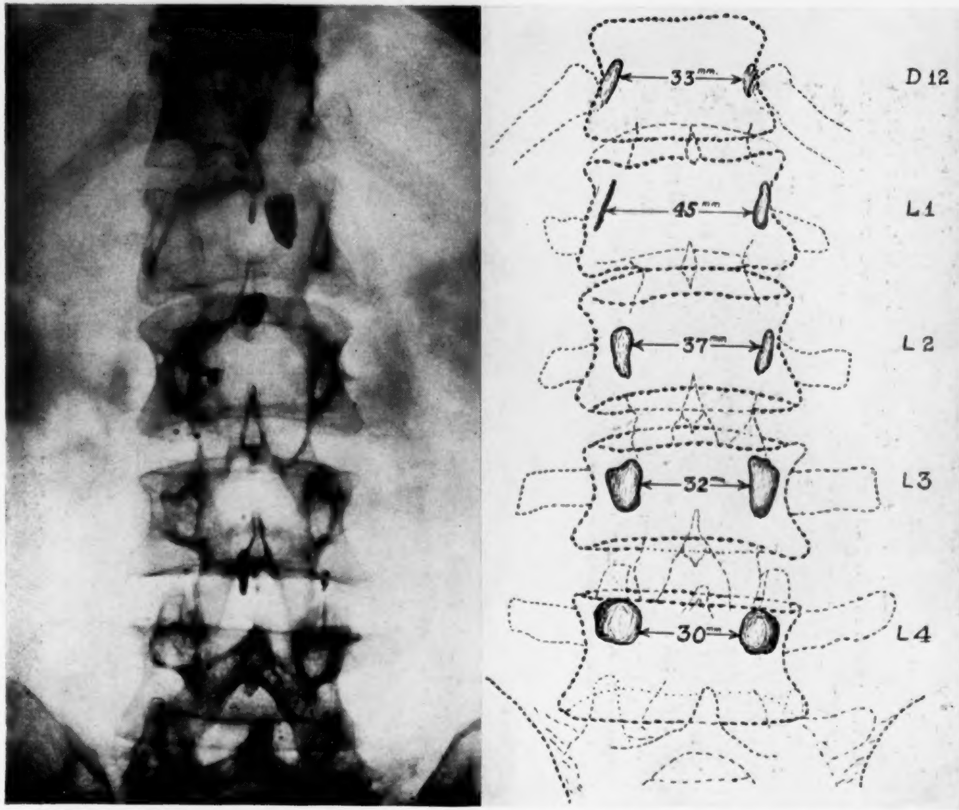

FIG. 1.—Roentgenogram showing enlargement of the spinal canal with atrophy of the pedicles of the twelfth thoracic and first, second and third lumbar vertebrae. Lipiodol seen above and below the lesion demonstrates the absence of a block in the cerebrospinal fluid.

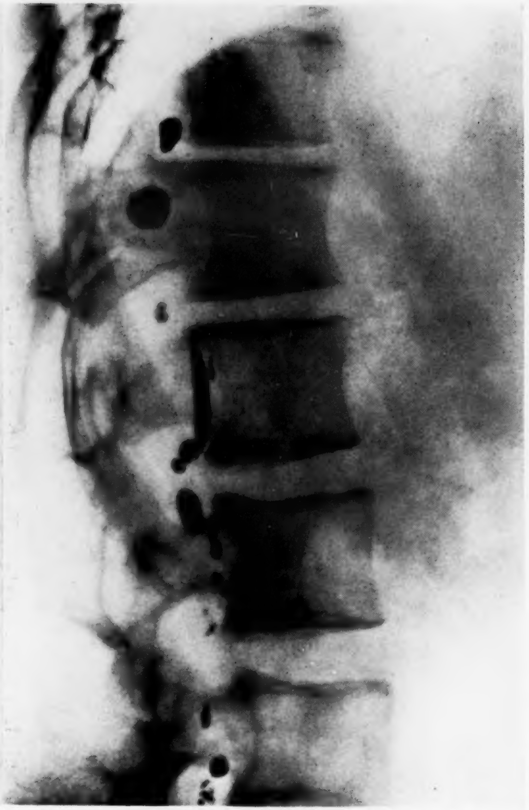

FIG. 2.—Roentgenogram of the lumbar vertebrae, lateral view, showing marked erosion of the dorsal surfaces of the vertebral bodies.

picture, so 1 cc. of lipiodol was then injected into the spinal canal. Subsequent developments showed that the use of lipiodol was unnecessary.

Roentgenologic Examination.—Upon examining the spine fluoroscopically the presence of an expanding intraspinal lesion was obvious, as the spinal canal was markedly widened at D_{XII}, L_I, and L_{II}, both in the lateral and anteroposterior diameters, and the pedicles were definitely atrophied. By tilting the patient under the fluoroscope the lipiodol was seen to meet an incomplete obstruction at L_I, where the column deviated to the left. The eccentric distribution of the lipiodol, above and below the lesion, proved the obstruction to be incomplete and thus accounted for the finding of a normal cerebrospinal fluid. The roentgenograms made at this time (Figs. 1 and 2) show the unusual degree of widening of the spinal canal. Upon measuring the interpeduncular spaces of the last thoracic and first three lumbar vertebrae, the vertebral canal was found to be from 2 to 15 Mm. wider than normal. The inner border of the pedicles of L_I and L were either flat or concave instead of the normal convexity shown at L_V. In the lateral view a marked erosion of the dorsal surfaces of the vertebral bodies was evident by their marked concavity.

Operation.—A laminectomy was performed April 11, 1935, by Dr. Percival Bailey, and the arches of the eleventh thoracic to the second lumbar vertebrae were removed. These were very thin and there was no epidural fat. A thin bluish membrane appeared immediately beneath the laminae. It was perforated and a clear fluid escaped. The extent of the cyst was then investigated and the sac was found to be enormous. It was necessary to extend the laminectomy from the tenth thoracic vertebra above to the fifth lumbar below before the complete dissection could be accomplished. Not until these two levels were reached was normal epidural fat encountered. The widest portion of the sac was at the level of the first lumbar vertebra. The cystic sac was easily dissected from the laminae and also from the dura mater. It was attached to the latter only at the first lumbar level by fibrous strands and blood vessels. There was no communication between the cystic cavity and the subarachnoid space. The dura mater was not opened. Doctor Bailey made the following statement in his operative report: "It was very interesting to look into this huge cavity to see how the bodies of the vertebrae had been eroded so that the intervertebral disks stood up like ridges between them."

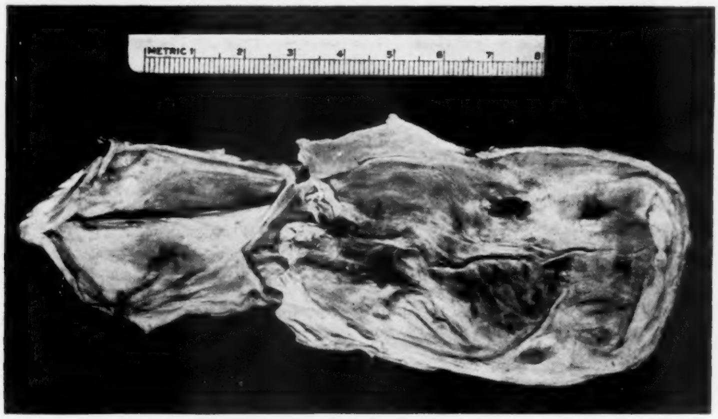

FIG. 3.—Photograph of the large extradural cyst removed at operation from the lumbar spinal canal.

Postoperative Course.—With exception of retention of urine for the first three days after the operation, the patient's recovery was speedy and uneventful. On the fourth day he was able to identify temperature and pin prick readily. He was discharged April 28, 1935, with mild spasticity of both lower extremities and weakness of extension of the legs, especially on the right. Six months after the operation he was quite well except for a slight limp and some weakness of the right leg. The sensation to vibration and position had returned in both the lower extremities.

Pathologic Examination.—Gross: The tissue removed at operation revealed a large cyst (Fig. 3) measuring 14 x 5 x 4 cm., in its greatest dimensions. The largest diameter was about 3 cm. from the upper end and from here it tapered off to a pointed lower end. The outside of the wall was smooth, grayish white, containing very few blood vessels. At either end were small amounts of fat. Four centimeters from the upper end, on the anterior surface, was a band of fibrous connective tissue containing a few medium sized blood vessels. This band was approximately 15 Mm. long. Upon opening the sac, the wall was found to be from 1 to 3 Mm. thick. The inner surface of the wall was smooth and glistening throughout. Across the junction of the middle and lower third of the cavity was a partial septum which appeared as though the sac may have had, at one time, two separate cavities.

Microscopic Examination.—The wall of the cyst seemed to be composed of two layers of fibrous tissue, a thin longitudinal outer layer and a much thicker circular inner layer. The tissue was a rather acellular collagenous connective tissue. There were very few blood vessels. In places a definite single layer of cells resembling endothelium could be seen lining the inner wall of the cyst (Fig. 4).

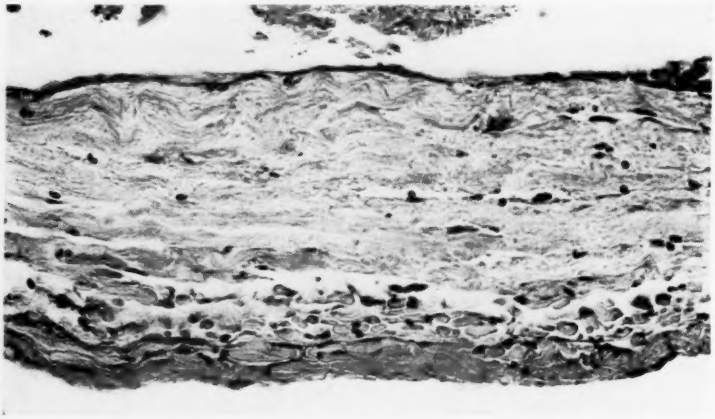

FIG. 4.—Photomicrograph of a cross-section of the cyst wall showing endothelial lining. Hematoxylin and eosin stain (×300).

DISCUSSION.—There were many interesting findings not recorded in other similar cases. The patient was a male, age 43, who had been perfectly well until two years before admission when he began to experience gradually increasing weakness and spasticity of both legs with muscular twitchings. It was not until nearly two years after the onset that he began having pain in the lower extremities, with change in the sensation of the skin and urinary disturbances. At no time, however, was pain the major complaint.

The changes in the motor system consisted of marked loss of power, muscular fibrillations and definite atrophy of the quadriceps muscles of both lower extremities, with symmetrically increased deep tendon reflexes. The Babinski sign was positive, and sustained ankle clonus could be obtained on the right side only. The motor involvement was in all probability due to indirect compression of the anterior surface of the spinal cord and roots against the hard bodies of the vertebrae by the fluid containing sac. This compression must have interfered with the pyramidal tracts more than the anterior horn cells, since spasticity was much more prominent than atrophy.

The sensory system was less involved than the motor system. Sensibility to pain, touch and temperature, with the exception of the twelfth thoracic dermatome, was only slightly impaired. However, sense of vibration and of position was completely lost in both lower extremities from the hips down. The widest portion of the cyst was located at about the level of L_I. The extreme lateral pressure on the twelfth thoracic posterior roots of the spinal cord had cut off all sensory pathways at this level, whereas the pressure below D_{XII} being not so great, the sensory changes below were only slight. The bulk of the cyst pressing directly on the posterior columns had probably impaired the vibratory and position sense early in the course of the illness.

It is difficult to explain why pain in these cases is so conspicuously absent, even when the lesion attains the enormous size it did in this case. Pain, when it is present with spinal tumors, is usually due to irritation of the posterior nerve roots. Absence of pain, then, in this case is all the more surprising since the twelfth thoracic roots had apparently been involved to such an extent as to produce complete anesthesia of the corresponding dermatome.

The extensive atrophy of the dorsal surfaces of the vertebral bodies would indicate that the cyst had gradually and progressively grown larger, probably from continued secretion of fluid within, exerting persistent pressure on the bony surfaces. It is therefore difficult to understand the absence of obstruction to the spinal canal in the presence of a tumor mass obviously large enough to completely fill the canal, as one would suppose from the eroded vertebral pedicles. However, that the cyst did not completely fill the spinal canal at all times is evident from the results of the lumbar puncture.

In Lewis' surgery extradural cysts are said to be either parasitic or dermoid in origin (with one exception which will be mentioned later). The cyst here reported belongs to another rarer group. They are thin walled sacs, either monolocular or multilocular, single or multiple, and filled with a clear, colorless fluid not unlike cerebrospinal fluid. The wall is composed of rather acellular fibers of connective tissue and has a lining of a single layer of flat cells resembling endothelium or the lining cells of the arachnoidal membrane. The cysts are attached loosely to the dura mater by thin fibrous bands which may be collected in a small pedicle or extend the full length of the cyst. The blood supply to the cyst usually comes from the dura mater through these bands.

The origin of these cysts is a matter of speculation. Elsberg, Dyke and Brewer suggest that they may have originated as a "congenital diverticulum of the dura mater" or "a herniation of the arachnoid through a congenital defect in the dura mater." Later the channel of communication becomes obliterated and reduced to a fibrous band, but the cyst continues to enlarge from a secretion of its own lining cells. The latter hypothesis is probably correct, for in one of the cases reported by Lehman the cyst did communicate with the subarachnoid space through a small patent pedicle and, when the cyst was opened, cerebrospinal fluid escaped. In all other cases reported, however, the small fibrous band of attachment to the dura mater was all that remained of the original pedicle.

After studying the four cases referred to in his pathologic material, Elsberg searched the literature for similar cases and found none. However, Lehman was able to find three other cases of extradural nonparasitic cyst possibly similar to those under consideration. They were reported by Schlesinger, in 1898, by Krause, in 1908, and by Mixter,[3] in 1932. The details concerning these cases are given by Lehman.[2] The two early cases are not very clear but that of Mixter, which appears in Lewis' surgery, seems to be identical with the present case. The cyst, however, was multilocular and extended from the third to the seventh dorsal vertebra. The symptoms began at the age of 12 (Table I).

TABLE I

RECORDED CASES OF SPINAL EXTRADURAL CYST

CASE NO.	DATE	REPORTED BY	AGE ON ADM.	DURATION OF SYMPTOMS	SEX AND COLOR	OPERATOR	LOCATION	NUMBER OF CYSTS FOUND	X-RAY EVIDENCE OF DILATATION OF SP. CANAL	VARIBILITY OF SYMPTOMS	RESULTS
1	1898	Schlesinger	?	....	?	None	Midthoracic	2	?	?	Postmortem finding
2	1908	Krauss	46	2 years	M.W.	Park	3rd to 6th dorsal	1	?	None	Incomplete cure
3	1932	Mixter	26	14 years	M.W.	Mixter	3rd to 7th dorsal	1	?	Marked	No Improvement
4	1934	Elsberg, Dyke Brewer: case 1	12	3 years	M.W.	Stookey	6th to 11th dorsal	1	Present	Marked	Incomplete cure
5	"	" case 2	15	3 months	M.W.	Elsberg	6th to 9th dorsal	1	"	None	Cured
6	"	" case 3	15	9 months	M.W.	"	5th to 9th dorsal	1	"	"	Incomplete cure
7	"	" case 4	16	2 years	F.W.	Taylor	Midthoracic	1	?	"	Cured
8	1935	Lehman case 1	12	3 months	M.C.	Lehman	6th to 9th dorsal	2	Present	Marked	Cured; Kyphosis
9	"	" case 2	17	9 months	M.C.	Bunch	6th to 10th dorsal	1	?	None	Cured; Kyphosis
10	1936	Cloward	45	2 years	M.W.	Bailey	11th dorsal to 4th lumbar	1	Present	"	Incomplete cure

The four cases of Elsberg, Dyke and Brewer were all in adolescents, all had symptoms of compression of the spinal cord, and all four cysts were located in the midthoracic region. The character of the cysts was entirely similar to the one herein described. They were attached to the outer surface of the dura mater only at a point near the exit of the posterior roots. Bony changes in the spinal canal were observed as in our case.

The two cases reported by Lehman were both in adolescents, the cysts also were in the midthoracic region and were typical pathologically. In each case the symptoms were marked by a predominance of motor involvement, with an incomplete sensory loss below the level of the lesion. One very significant observation made in Lehman's first case was the fluctuation of symptoms, particularly exacerbation and remission of the subjective complaints. It was in this case that the patent channel of communication between the cyst and the subarachnoid space was found. Lehman supposed that these cysts fill out and empty intermittently, thus changing the degree of pressure on the spinal cord from time to time. When this channel closes permanently and the lining of the cyst continues to secrete, the symptoms then progress steadily with the expanding of the sac. This intermittency of symptoms early in the clinical course is offered by Lehman as being of diagnostic significance.

Elsberg has formulated what he calls a "characteristic syndrome" of compression of the spinal cord by an extradural cyst which includes the following: "The individual is an adolescent; the tumors are usually found in the midthoracic region, *i.e.*, between the 4th and 10th thoracic vertebrae; the manometric tests demonstrate a subarachnoid block with characteristic spinal fluid changes of cord compression; and pain is absent or not a prominent symptom."

In our case there may be some connection between the location of the cyst and the age of the patient. All certain cases heretofore reported were found in the midthoracic region and all in adolescents. There is a possibility that when the cyst is located in the lumbar region, where the spinal canal is larger in all its dimensions, it may develop for a longer period before producing symptoms.

From the findings in our case we may conclude that spinal extradural cysts may be found also in adults, that they may be located also in the lumbar region, and that even though they reach an enormous size there may be a normal manometric test and no changes in the spinal fluid. The enlargement of the spinal canal with atrophy of the pedicles as seen in the roentgenograms, and the relative absence of pain seem to be the only findings that are common to all cases. These are by no means pathognomonic, however, as they may be observed also in other tumors within the spinal canal, both extramedullary and intramedullary.

REFERENCES

[1] Elsberg, C. A., Dyke, C. G., and Brewer, E. D.: The Symptoms and Diagnosis of Extradural Cysts. Bull. Neurol. Inst. New York, **3**, 359–417, March, 1934.

[2] Lehman, E. P.: Spinal Extradural Cysts. Amer. J. Surg., **28**, 307–322, 1935.

[3] Mixter, W. J.: Practice of Surgery, Pryor. Ed. by Dean Lewis. **12**, Chap. iii, 52–68, 1932.

SACROCOCCYGEAL TERATOMA*

J. Arnold deVeer, M.D., and Jefferson Browder, M.D.
Brooklyn, N. Y.

FROM THE DEPARTMENTS OF PATHOLOGY AND SURGERY, LONG ISLAND COLLEGE OF MEDICINE, BROOKLYN, N. Y.

The sacrococcygeal region is a common site for the occurrence of a variety of fistulae, cysts and tumors. Because of the multiplicity of possible factors in their derivation and the variability of their structure, no rigid classification of these lesions has as yet been effected. Many of them are relatively common (pilonidal cysts and sinuses, sacral meningomyeloceles,† *etc.*) and seldom offer diagnostic difficulties. Much less frequent are the teratomatous tumors which in rare instances have been described as an integral part of an anomaly of the neural canal. These in general are the tumors presenting on the dorsal aspect of the sacrum. Another group, histologically similar, have no important connections with the spinal cord or its membranes but are attached to the coccyx or distal portion of the sacrum. They lie chiefly in front of the sacrum and coccyx but, when large, protrude posteriorly and resemble superficially the sacral meningomyeloceles. Three cases of this type herein reported were in fact, referred to one of us (J. B.) with the diagnosis of meningocele.

We are presenting four cases of sacrococcygeal teratoma and, for comparison, one example of sacral meningomyelocele to illustrate the respective diagnostic features. The relative ease with which the teratomata were extirpated, and the excellent results obtained, contrast strikingly with the difficulties and discouraging prognosis usually attendant upon the surgical treatment of the sacral meningomyeloceles.

Case Reports

Case 1.—H. C., a two months old male, was admitted to the Pediatric Service of Dr. Carl Laws at the Long Island College Hospital February 10, 1925. He was the fourth child of normal parents. At birth two small lumps were present over the lower end of the spine but subsequently they gradually became larger and fused into a single tense tumor which "felt as if it had fluid inside it." No weakness of the lower extremities had been observed nor were there any urinary or rectal difficulties.

Physical Examination.—There were no abnormalities other than a large tumor attached to the buttocks (Fig. 1). The mass was covered with true skin, its surface was lobulated and its base sessile, displacing the anal orifice to the left. The lobulations were fairly soft, seemed cystic but could not be reduced. Rectal examination disclosed a smooth elastic tumor filling the pelvic outlet to such an extent that the examining finger impinged upon the under surface of the symphysis pubis. The external anal sphincter appeared normal. No cutaneous sensory disturbances could be demonstrated over the buttocks, and the lower extremities showed no abnormalities of function. When the child cried the mass did not increase in size or become more tense. Roentgenologic examination showed the coccyx to be displaced posteriorly.

---

* Read before the New York Surgical Society, April 8, 1936. Submitted for publication September 8, 1936.

†The term meningomyelocele is employed throughout this paper to indicate not only this specific anomaly but also the related meningoceles, the syringomyeloceles and the syringomeningomyeloceles.

Operation.—By Dr. Emil Goetsch. Under ether anesthesia, the base of the tumor was outlined by an elliptical cutaneous incision leaving the skin covering the tumor in situ. By sharp and blunt dissection the mass was freed from the surrounding structures without difficulty. The tumor was found to be attached to the coccyx which was therefore amputated at the sacrococcygeal junction. There was no demonstrable attachment elsewhere. The wound was closed without drainage. There was an immediate postoperative rise of temperature to 104.2° F. which gradually subsided during the following three days. A small area of the wound was superficially infected but slowly granulated and at the end of a month was completely healed. The child was discharged from the hospital April 7, 1925, in excellent condition.

Pathologic Examination.—*Gross:* The specimen consisted of a coarsely lobulated mass covered in part by normal skin. It measured approximately 12 x 10 x 6 cm. On section it was found to contain several irregular shaped cavities filled with straw colored fluid. These cavities had smooth lining surfaces and their walls were trabeculated. The solid portions were divided into nodules of varying consistency, separated by connective tissue septa. No parenchymatous tissue could be identified as such. *Microscopically* the solid portions of the tumor consisted mainly of lobulated masses of brain tissue with varying degrees of gliosis. An occasional island of bone formation was noted. Scattered in an irregular manner were clusters of cells suggesting compound racemose glands. The cystic spaces were lined with epithelium, resembling bronchial and gastro-intestinal mucosa. Interspersed throughout was much adipose and connective tissue.

Five years later, in April, 1929, it was reported that the child was living and well with no evidence of recurrence of the tumor.

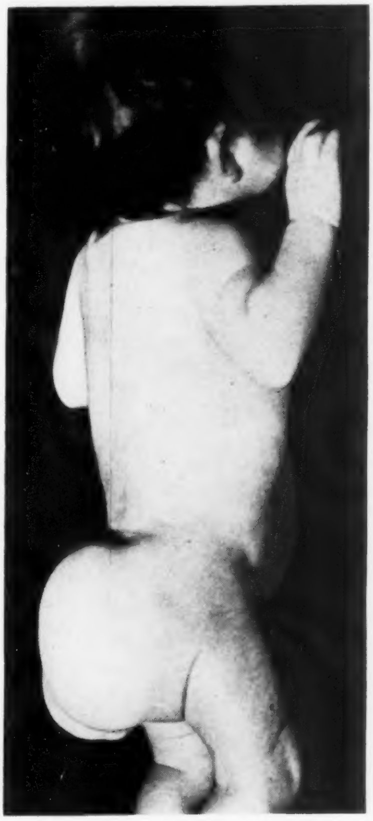

FIG. 1.—(Case 1.) An example of a sacrococcygeal teratoma with a moderately large externally visible portion.

Case 2.—R. T., a three months old female, was admitted to the Surgical Service of Dr. Emil Goetsch at the Long Island College Hospital July 30, 1925. This was the second child of normal parents. It had been delivered by a midwife who noticed a small tumor over the lower end of the spine. This mass was soft and covered with normal skin. There were no abnormalities of the lower extremities. There had been slight increase in the size of the mass since birth.

Physical Examination.—The child was well developed and weighed 12 pounds. Nothing of importance was noted except in the coccygeal region where a round mass could be seen. The overlying skin was freely movable and showed no discoloration. Bimanual palpation with a finger in the rectum disclosed an oval shaped resilient mass about the size of a small lemon apparently attached to the coccyx. There was no increased tension of this structure during forceful crying nor could its contents be reduced. The external anal sphincter seemed normal. No cutaneous sensory changes or motor weakness of the lower extremities could be demonstrated.

Operation.—Under ether anesthesia, the mass was exposed through a transverse cutaneous incision. It was ovoid in shape, had a smooth surface, and at its cephalad end was fused with the first coccygeal segment. The remainder of the coccyx could not be identified as such. The tumor with the involved coccyx was amputated at the sacrococcygeal articulation. The wound was closed without drainage. Shortly after operation the temperature rose to 104° F. but returned to normal within 24 hours. The remainder of the patient's stay in the hospital was uneventful and she was discharged August 16, 1925.

Pathologic Examination.—Gross: The specimen consisted of an oval shaped mass measuring 6 x 4 x 3 cm. On section it was found to be composed of a solitary cyst with a smooth glistening lining and an irregular intramural nodule 2 x 3 x 2 cm. The cut surface of this nodule was grayish white and appeared to be composed of cellular areas and connective tissue septa.

Microscopic.—Throughout, numerous small islands of brain tissue were distributed. In close proximity to one of the larger areas of brain structure there was a pouch lined by squamous epithelium. In other areas convoluted glands lined with ciliated columnar epithelium were seen. The lining of a number of small cystic spaces resembled gastrointestinal mucosa.

Recent examination showed a normal girl now ten years old, without any demonstrable abnormalities.

Case 3.—S. B., a ten day old female, was born at full term in the Methodist Episcopal Hospital June 15, 1932. Following the delivery there was seen a large lobulated tumor protruding from the region of the buttocks and displacing the anal orifice to the left. During the next ten days the mass grew appreciably larger. The infant urinated and defecated in a normal manner. No disturbance of the function of the lower extremities was noted.

Physical Examination.—The child was a well developed and well nourished female infant with a prominent tumor mass protruding from the region of the right buttocks, approximately one-third the size of the infant's trunk, and completely covered with normal skin. On transillumination shadows could be seen which suggested septa between several cystic lobules. Rectal examination disclosed that the mass extended into the pelvis and almost completely filled its outlet. The anal sphincters functioned normally. No sensory or motor changes could be demonstrated.

Operation.—June 28, 1932. Under local anesthesia an elliptical incision was made about the base of the mass. By dissection, it was easily freed from the surrounding structures. A solid portion was fused with the coccyx necessitating division of the sacrococcygeal articulation. The wound was closed without drainage. There was a sharp postoperative rise of temperature to 103° F., but otherwise the postoperative course was uneventful. At the close of the operation a transfusion of blood was given.

Pathologic Examination.—Gross: The specimen measured approximately 22 x 12 x 10 cm. Its surface was irregular and the larger lobules had thin bluish semitranslucent walls. It appeared that about one-third of the mass was made up of solid tissue. Unfortunately the specimen was lost without further examination being made.

The child returned recently for examination and was found to be normal except for considerable atrophy of the buttocks, more marked on the right side (Fig. 2).

Case 4.—J. S., a six months old male, was admitted to the Kings County Hospital August 28, 1935. At birth there was observed a protrusion about the size of a lemon situated just dorsal to and slightly to the right of the anus. It had grown much larger in the interval and displaced the anus to the left side. For three months there had been a moderate degree of constipation relieved by enemata. No urinary disturbance or weakness of the lower extremities had been noticed.

Physical Examination.—The findings were unimportant except for the presence of a rounded mass about the size of the infant's head attached by a broad base to the region of the buttocks. This could not be reduced nor was there any increase in its size when the child cried. The external anal sphincter was functioning but there was leakage of fecal material due to its being stretched. The urinary apparatus seemed normal. No motor or sensory disturbance was demonstrable in the lower extremities.

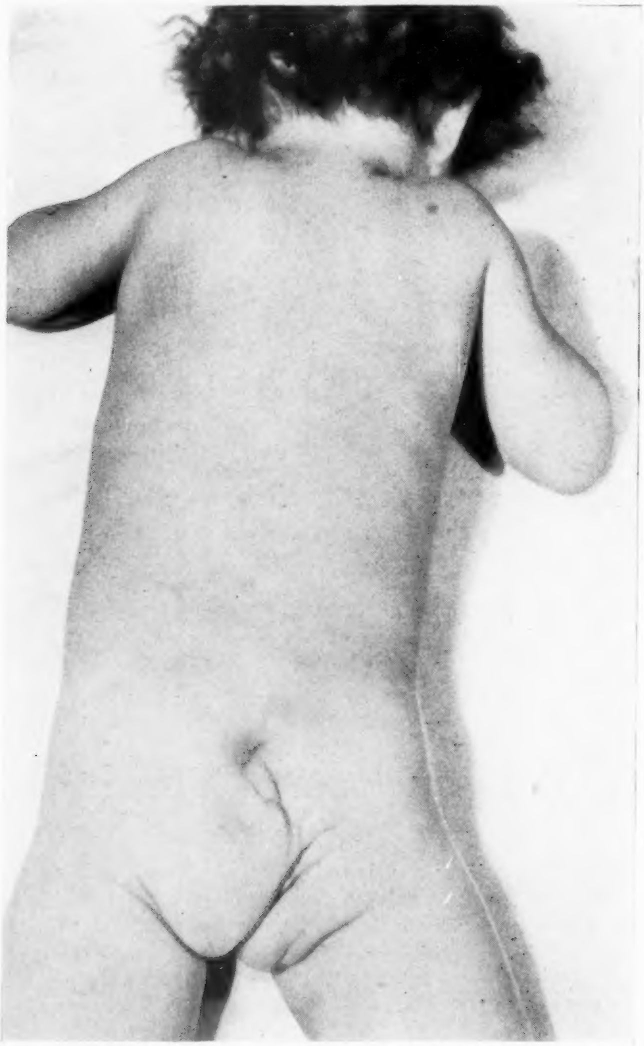

FIG. 2.—(Case 3.) Four years after operation showing atrophy of the buttocks.

Roentgenologic examination of the pelvis showed opaque structures in the mass resembling rudimentary phalanges.

Operation.—August 3, 1935. Under ether anesthesia an elliptical incision was made about the dome of the tumor. The right gluteus maximus muscle was atrophic. The mass was easily dissected from the surrounding structures and was found to be firmly attached to the coccyx. The sacrococcygeal articulation was therefore divided. The wound was closed with drainage. At the end of the operation a transfusion of blood was given. There was a sharp postoperative rise in temperature to 105° F. which returned to normal on the third day; the subsequent course in the hospital was uneventful.

Pathologic Examination.—Gross: The excised mass (Fig. 3) was irregularly ovoid and was partially covered by normal skin. It measured 13 x 10 x 9 cm. Immediately beneath the skin was a large dermoid cyst filled with cheesy material which comprised the greater part of the entire tumor. A nodule of solid tissue, protruding into the cyst, was covered by epidermis with a macerated surface. From this nodule a number of long hairs projected into the cyst cavity. The remainder of the tumor was continuous with the dermoid anlage and lay just outside of the superior pole of the large cyst. This portion was composed of solid gray white tissue in which numerous small cystic cavities were distributed. The latter contained, for the most part, translucent gelatinous material. Several nodules of bone were also encountered on sectioning the tissue. *Microscopic* examination of various portions of the tumor (Fig. 4, A, B, C, D) showed structures clearly identifiable as gastric and intestinal mucosa, pancreatic tissue, gliotic brain tissue, choroid plexus, and salivary glands. There were also islands of bone with active bone marrow, cartilage, smooth muscle, myxomatous and adipose tissue. The large cyst contained desquamated epithelium, hair and the secretions of dermal glands situated in the solid portion of its wall. The smaller cysts were derived from mucus secreting epithelial membranes of various types.

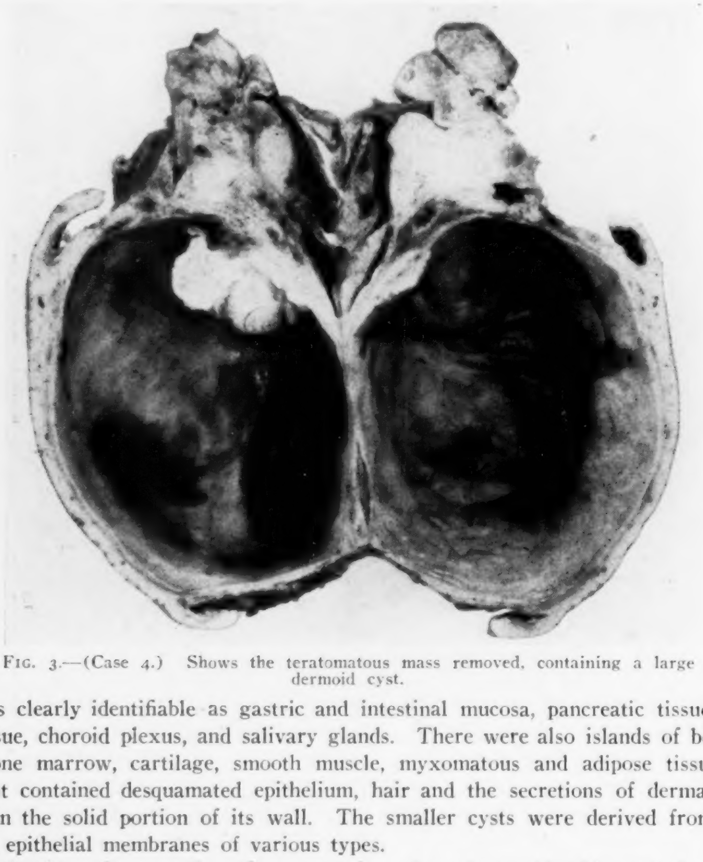

Fig. 3.—(Case 4.) Shows the teratomatous mass removed, containing a large dermoid cyst.

Examination nine months after operation showed considerable atrophy of the buttocks, more marked on the right side. Otherwise the child was well developed and appeared in perfect health.

Since this paper was submitted for publication J. S. (Case 4) was readmitted to the hospital with mild abdominal distention and inability to defecate. Rectal examination disclosed a hard, fixed mass encircling the rectum just within the internal anal sphincter. The extent of the mass could not be determined. There was a rapid growth of this obviously malignant tumor during the next two months and death occurred November 20, 1936. Autopsy disclosed extensive invasion of the pelvis, buttocks and retroperitoneal lymph nodes. Histologically the tumor was found to be of undifferentiated cell type and was interpreted as an embryonal carcinoma.

Case 5.—S. S., a three year old male, was admitted to the Kings County Hospital January 10, 1934. At birth there was noted a small protruding mass at the lower end of the spine, which was soft and had a bluish color. The mass had remained about the same size since birth. There had been urinary and fecal incontinence. The child had never been able to walk without assistance. He was brought to the hospital because of the urinary incontinence.

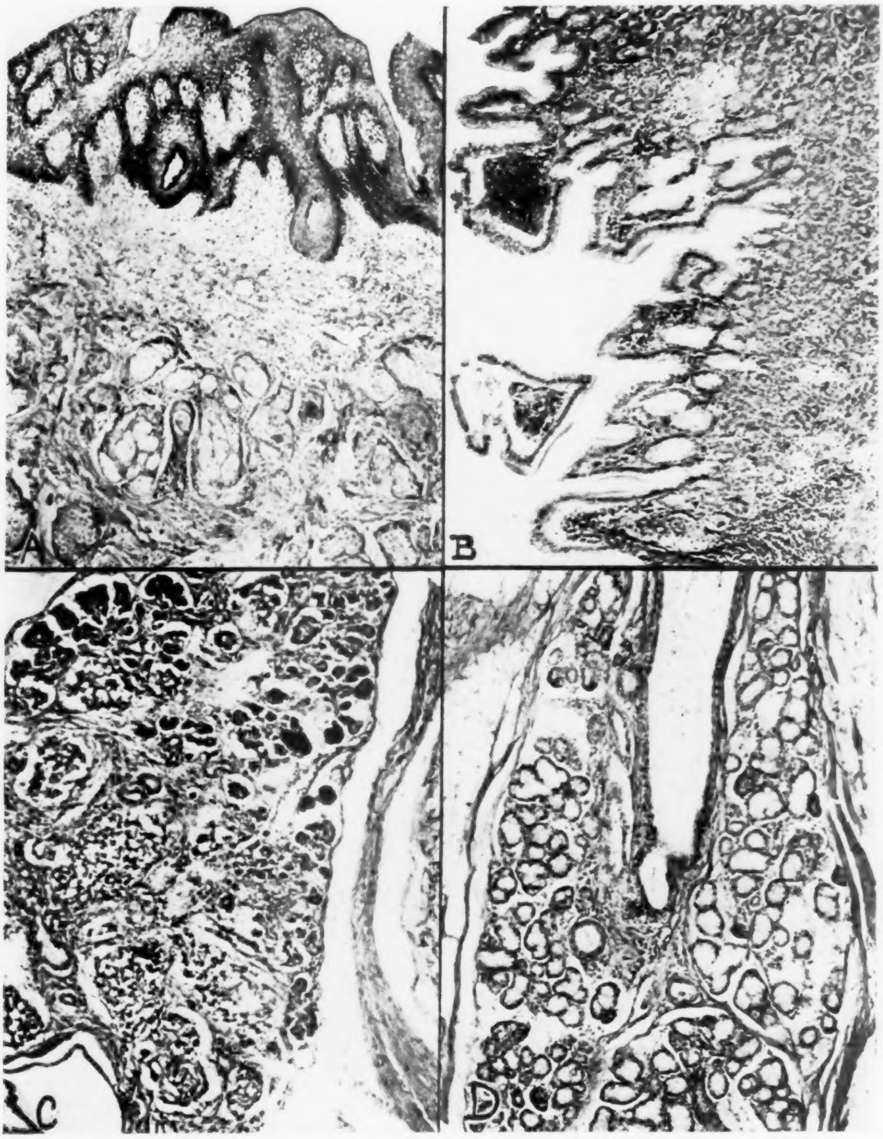

Fig. 4.—Photomicrographs of portions of the specimen shown in Fig. 3. (A) Skin with dermal glands and hair follicles from the dermoid anlage. (B) Gastric mucosa. (C) Pancreatic tissue. (D) Mucus secreting glands probably belonging to the salivary apparatus.

Physical Examination disclosed an undernourished, pot bellied, markedly dehydrated child with a rounded tumor in the region of the sacrum (Fig. 5). The head, upper extremities and trunk presented no unusual findings. The sacral mass was covered over its distal portion with scaly, embryonal skin. The mass was cystic, could be partially reduced and became quite tense when the child cried. A bony defect in the sacrum was easily palpable. The anal orifice was open and no contraction of the external sphincter was noted. The thighs and legs could be voluntarily flexed and extended but there was no voluntary control of the feet. Complete cutaneous anesthesia and analgesia could be demonstrated from the first sacral dermatome downward.

Operation.—Under ether anesthesia, the mass was explored and there was found an embryonal spinal cord attached to the dome of the meningocele cavity. Atrophic spinal nerves passed from this cord through the sacral foramina. The spinal cord was detached and the sacral defect repaired. On the third postoperative day there developed evidences of meningitis from which the child died two days later.

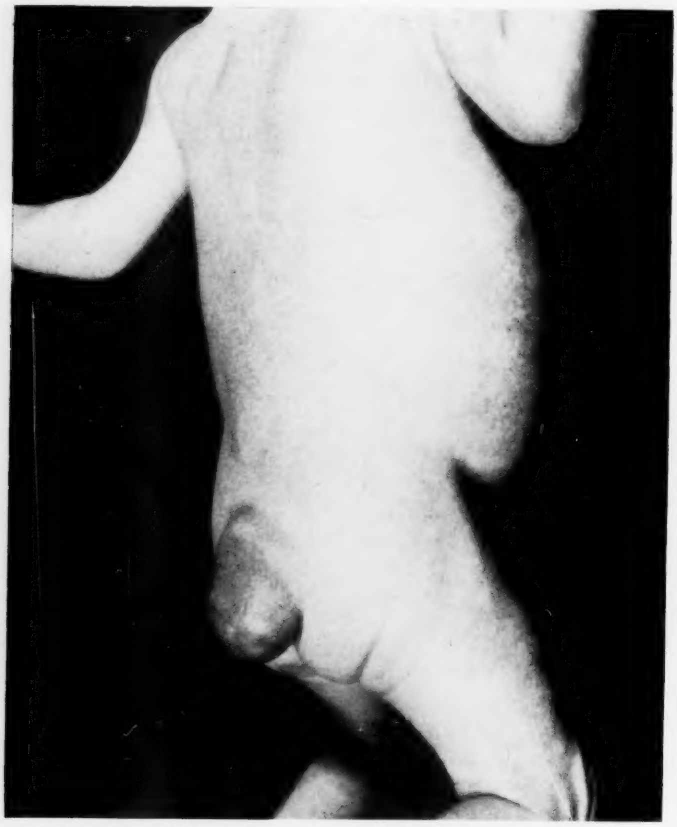

FIG. 5.—(Case 5.) A sacral meningomyelocele, included for comparison.

Pathologic Examination.—Gross: The specimen consisted of a portion of the wall of a meningomyelocele, covered on its outer surface by wrinkled embryonal skin and on its inner surface by a glistening membrane. Beneath the lining was seen an area of tissue resembling a prolongation of the spinal cord. *Microscopically* there was seen a mass of nerve tissue containing scattered groups of ganglion cells, irregular fiber tracts and patches of glial overgrowth, the latter projecting into the surrounding connective tissue. One surface was covered by atrophic skin.

Discussion.—The subject of malformations and new growths in the sacrococcygeal regions has occupied a prominent position in medical literature of the past 50 years. To attempt a review of the large volume of accumulated data and discussions pertaining to the subject seems unwarranted. The reader is therefore referred to articles by von Bergmann,[1] von Recklinghausen,[2] Kummel,[3] Mallory,[4] Borst,[5] and Schwalbe.[6] A variety of local embryonal structures have been drawn upon to explain the origin of the various fissures, fistulae, cysts and tumors so common in this region. Among these are the fovea coccygea and the coccygeal vestiges of the neural canal, the neurenteric canal, the postanal gut and the proctodeal membrane. According to Ewing,[7] although some of the tumors may, with considerable certainty, be referred to single embryonal structures, the majority of them are more complex and probably involve more than one of these embryonal remnants or some additional anomalies of development. The concept that teratomata may arise from parthenogenetically developing sex cells, a modification of the old "bigerminal theory," has been given much support by the researches of Bosaeus[8] on the origin of ovarian embryomata. He removed from frogs' ovaries unfertilized ova, pricked them with a needle, as Jacques Loeb had done, to stimulate parthenogenetic development, and then reimplanted them into the lymph sac, pleural cavity or ovary of the particular frog from which they had been taken. From these ova complicated teratomata developed that had "essentially the same stucture as the spontaneous adult teratomata or cystic embryomata." MacCallum[9] favors this explanation for the development of teratomata of the gonads where they are often accompanied by chorionic membranes, but holds that the teratomatous tumors in the sacrococcygeal region and brain which approach the complexity of twin inclusions, and even the simplest cysts composed of only one or two types of tissue, are best explained as originating from isolated somatic blastomerés with varying potentialities. A teratoma resulting from parthenogenetic development of a sex cell would be of the nature of an offspring while one derived from an isolated blastomere would be of the same generation as the host, a twin.

It is generally recognized that teratomata such as we have described are benign growths but that one of their component tissues may undergo malignant degeneration. In reporting a case of "Sacrococcygeal Carcinomatous Teratoma," Stewart, Alter and Craig[10] comment that malignancy in such lesions in childhood is either not as common as it is generally thought to be or the cases have not been reported, for they were able to find only four other instances in the literature. These authors quote a statement by Gant[11] to the effect that teratomata in this region show a tendency to undergo cancerous degeneration unless excised early. Renner and Goodsitt[12] have recently reported the case of an infant from whom a "tail-like mass," a teratoma, was removed shortly after birth. The tumor did not appear to extend into the pelvis and no pelvic mass was palpable at that time. Ten months later the child developed constipation and inability to void, and was found to have a large malignant teratoma located between the rectum and the sacrum and infiltrating the rectal wall. The intrapelvic tumor, which these authors considered as a second or independent tumor, could probably have been successfully extirpated had it been recognizable at the time of removal of the externally visible mass.

Early complete excision of these tumors is indicated as a prophylaxis against malignant change if for no other reason. Also the external portions are not only unsightly but easily vulnerable, while the intrapelvic portions, which are frequently the larger, may cause various pressure effects.

The meningoceles, meningomyeloceles and meningosyringomyeloceles are all the result of defective development of the neural canal. The protruding mass may show a superficial resemblance to the sacrococcygeal teratomata but the two classes of lesions can usually be differentiated by the following features.

DIFFERENTIAL DIAGNOSIS.—(1) The skin covering of the teratomata is true skin whereas the meningomyeloceles are usually covered with thin "embryonal skin" which is easily eroded and ulcerated.

(2) The teratomata vary widely in size. They may protrude but slightly from the pelvis, indeed may be entirely intrapelvic, or present as huge external masses the size of the infant's head or larger, with a palpable intrapelvic portion as well. The meningomyeloceles, on the other hand, are seldom so large and, except in the case of the rare "anterior meningoceles," there is no extension into the pelvis.

(3) A rapid increase in the size of the teratomata is usually noted in the early months of life. This, according to Hansmann and Berne,[13] parallels the growth of the infant and should not be taken as evidence of malignancy. The meningomyeloceles show no such rapid increase in size.

(4) Most of the teratomata can be recognized as containing both solid and cystic portions. They are not reducible and show no enlargement or increased tension when the child cries, or when the jugular veins are compressed. The meningomyeloceles are distinctly cystic and show the various evidences of communication with the spinal subarachnoid space.

(5) The teratomata are associated with no motor or sensory disturbances except, in rare instances, where the tumor presses on the lumbosacral plexuses. The cases of the meningomyelocele group are commonly characterized by loss of sphincteric control and sensory and motor disturbances of the buttocks and the lower extremities.

(6) Hydrocephalus is not encountered in cases of sacrococcygeal teratoma whereas it is often present in the examples of meningomyelocele, particularly after surgical removal of the meningocele sac.

OPERABILITY.—Regarding the operability of sacrococcygeal tumors, we are aware of the fact that not all of the cases offer the favorable outlook of those we are reporting. In each of our four cases the tumor was composed of well differentiated tissues in which no evidence of malignant degeneration was found. In each instance there was no associated spinal cord or spinal canal anomaly, the tumor was not attached to other important structures and excision was accomplished without great technical difficulty. The fact that all four cases were in infants with tumors externally visible at birth, made early diagnosis and early operation possible. When this is not the case such tumors may go unnoticed until adult life when symptoms of compression of pelvic structures may develop as a result of sudden growth activity. Some of the cases in the group reported by Hundling[14] were undoubtedly of this type. Teratomatous masses have been encountered in association with spina bifida occulta (von Recklinghausen[2]). Keen and Coplin[15] found a fistulous tract passing through a defect in the sacrum and communicating with the rectum in a case of sacrococcygeal teratoma. Such cases present very different surgical problems from those encountered in our series.

CONCLUSIONS

We are of the opinion that a large majority of the sacrococcygeal teratomata in infants are benign, that they can be clinically differentiated from the cases of the meningomyelocele group, and that they are not attached to important structures and should therefore be operated upon as early as possible with the expectation of good functional results. The only residual abnormality to be expected is atrophy of the gluteal muscles in instances where the tumor is very large.

REFERENCES

[1] von Bergmann, E.: Berl. klin. Wchnschr., **48,** 761, 780, 1884.
[2] von Recklinghausen, F.: Virchows Arch. f. path. Anat., **105,** 243, 373, 1886.
[3] Kummel, W.: Virchows Arch. f. path. Anat., **118,** 37, 1889.
[4] Mallory, F. B.: Am. J. M. Sc., **103,** 263, 1892.
[5] Borst, Max: Centralbl. f. allg. Path. u. path. Anat., **9,** 449, 1898.
[6] Schwalbe, E.: Die Morphologie der Missbildungen des Menchen und der Tiere I Teil: Allgemeine Missbildungslehre. G. Fischer, Jena, 1906.
[7] Ewing, J.: Neoplastic Diseases. W. B. Saunders Co., Philadelphia, 1928.
[8] Bosaeus, W.: Genese d. Ovarialembryome. Akad. Abhandl., Uppsala, 1926. Quoted by MacCallum.
[9] MacCallum, W. G.: Text-book of Pathology. W. B. Saunders Co., Philadelphia, 1932.
[10] Stewart, J. D., Alter, N. M., and Craig, J. D.: Surg., Gynec. & Obstet., **50,** 85, 1930.
[11] Gant, S. G.: Diseases of the Rectum and Colon, **2,** 263. W. B. Saunders Co., Philadelphia, 1923. Quoted by Stewart, Alter and Craig.
[12] Renner, R. R., and Goodsitt, E.: Am. J. Cancer, **24,** 217, 1935.
[13] Hansmann, G. N., and Berne, C. J.: Arch. Surg., **25,** 1090, 1932.
[14] Hundling, H. W.: Surg., Gynec. & Obstet., **38,** 518, 1924.
[15] Keen, W. M., and Coplin, W. M. L.: Surg., Gynec. & Obstet., **3,** 661, 1906.

CANCER OF THE TONGUE

A REPORT OF ONE HUNDRED AND EIGHTY-SEVEN CASES, WITH AN ANALYSIS OF NINETY-EIGHT TREATED PRINCIPALLY BY SURGERY AT THE NEW YORK SKIN AND CANCER HOSPITAL BETWEEN 1917 AND 1935

ALBERT S. MORROW, M.D.
NEW YORK, N. Y.

FROM THE SURGICAL SERVICE OF THE SKIN AND CANCER UNIT OF THE NEW YORK POST-GRADUATE HOSPITAL (FORMERLY THE NEW YORK SKIN AND CANCER HOSPITAL), DR. CARL EGGERS, DIRECTOR

THE treatment of tongue cancer at the Skin and Cancer Unit of the New York Post-Graduate Hospital is based on the belief that thorough surgical removal of the tongue lesion by the knife or the electrocautery, combined with a block dissection of all the superficial and deep cervical nodes, whether clinically showing evidence of metastases or not, is the most rapid and effective means of eradication and gives the greatest assurance of freedom from recurrence. At the same time, the value of radiotherapy in certain cases is well recognized, but, in general, radium and roentgen ray are reserved for the more radiosensitive types of tumors, for cases upon whom prolonged operative procedures are contraindicated, either on account of the age or condition of the patient or the location and extent of the lesion, and as a palliative measure for hopeless cases.

For the purpose of determining the results these principles of treatment were giving, a study of the records of tongue cancer treated during the last 19 years was undertaken. A review of the literature on cancer of the tongue for the last five years was also made, mainly with a view of comparing our own results with those of other institutions devoted to the treatment of cancer. This study, however, has not proved as helpful as was anticipated, first, because the material upon which statistics are based must necessarily vary in different groups, and secondly, on account of the lack of uniformity in the methods of compiling statistics. The chief difficulty in this respect arises from the failure of everyone to adopt a uniform interval following treatment in reporting so called "cures." Another source of confusion lies in the fact that many writers group their tongue cases with cancers of other parts of the mouth under the heading of intra-oral or mouth cancer, and include with tongue cases cancers of the cheek, gums, tonsils, soft palate, and often cancer of the lip. While it is true that mouth cancers are usually of the squamous cell type, yet in different locations they vary as to the malignancy and their response to radiation, and, what is more important, the rapidity with which they metastasize and the paths along which metastases occur. Thus, to compare the results of one method of treatment employed in a group of tongue cases alone, with some different form of treatment applied to a group in which are

---

Submitted for publication, July 27, 1936.

included cancers from other parts of the mouth, can result only in misleading conclusions.

One fact that stands out from even a cursory review of the voluminous literature on the subject is that authorities are far from being in accord on the treatment of tongue cancer. Surgery, electrosurgery, and radium are each advocated for the treatment of the tongue lesion by their supporters, while for the treatment of the lymphatics draining the area involved we find such a variety of procedures employed that one is quite bewildered. There is no doubt that in recent years there has been a very definite trend from surgery toward the use of radium in the treatment of the cervical nodes as well as the tongue lesion. For this reason, it was thought a report of the results in an unselected group of tongue cancers which were, for the most part, advanced, and in which the treatment with few exceptions was surgical, would be of interest.

Among the files of malignant tumors of the tongue examined or treated at this hospital during the period from 1917 to 1935, inclusive, there were 202 cases listed under carcinoma and two under sarcoma. Eighty-eight of the patients had a clinical diagnosis only, while in 114 the diagnosis was confirmed by biopsy or a complete tissue examination after operation. All of the latter were of the squamous cell type, except one lympho-epithelioma. Three cases were associated with other cancers. In one there was also a squamous cell carcinoma of the upper lip and a basal cell carcinoma of the back. Another had, in addition to the tongue lesion, a basal cell carcinoma of the nose. In the third case, there was also a carcinoma of the breast (clinical diagnosis only).

The correctness of the clinical diagnosis appears doubtful or was later disproved in six cases. In three of these, the lesion healed after extraction of teeth, two of them being followed for one year and three years, respectively, without recurrence. A fourth case was treated for syphilis and at the end of a year showed no pathology of the tongue. The histologic report on a fifth case, after hemiglossectomy, was a tuberculous ulcer of the tongue. The sixth case had a part of the tongue and floor of the mouth removed and a bilateral cervical node operation, the pathologic examination showing only inflammatory changes. Nine others were either primary carcinomata of the tonsil or floor of the mouth which had spread to the tongue.

Many of the remaining 187 cases were far advanced or inoperable when they applied for treatment. In 31 histories from the entire group, it is definitely stated that the cases were inoperable, but there are at least 32 others which, from the description of the lesion or the condition of the cervical nodes, should be classed as such, giving a total of 63 (33 per cent) that were inoperable when they came to the clinic. If the criteria of inoperability laid down by Quick[1] and others, such as the presence of bilateral palpable nodes, were followed, the percentage of inoperable cases would be considerably higher. Thirty-nine (20 per cent) gave a history of having received some form of previous treatment, such as cauterization, the use of radium, or incomplete operation.

UNTREATED CASES.—Fifty of the 187 cases were disposed of as follows: Twenty-two were admitted to the hospital and discharged within a few days without receiving any treatment. Half of these were signed out as inoperable. There were no reasons stated why the remaining cases were not treated, but, from an examination of the histories, it is evident that many of them were in a similar condition. Seventeen were advised to enter the hospital for treatment, but failed to do so or went elsewhere; eight were sent to other hospitals for radiotherapy; two were sent direct to a home for incurables; and one died while in the hospital.

INOPERABLE CASES TREATED BY RADIOTHERAPY.—Thirty-four cases were treated solely by roentgen therapy or radium. The majority of these patients were in an advanced or inoperable stage of the disease, and were referred to the radiotherapy department for palliative treatment. As there were no five year survivals among this group, all cases from 1917 to 1935 are considered together.

Nine of the patients were 70 years of age or over. Six were described as cachectic, "losing weight," or in poor general condition. Eight had positive Wassermanns, and another gave a history of previous syphilitic treatment. Eight gave the duration of the lesion as one year or over. Fourteen were secondary cases. Ten of the 34 involved the base of the tongue. In 13 cases the disease had spread beyond the tongue onto the floor of the mouth, tonsil, or epiglottis. Twenty-six of the group had palpable nodes, ten showed bilateral involvement. Some of these were described as hard and fixed, and in one ulceration had taken place. In only 12 of the 34 cases was the diagnosis confirmed by a biopsy. Of these, there were seven Grade 1, two Grade 2, and two Grade 3 tumors; one was not graded. There was one lympho-epithelioma in the group, a Grade 2 tumor with palpable nodes.

Nineteen cases were treated by interstitial radiation alone or in combination with external radiation by the roentgen ray. Fifteen were treated solely by external radiation with the roentgen ray. Six of the latter were sent to homes for incurables after one or more treatments; three of these have died since. One died in the hospital from uremia two days after the insertion of radium needles. Nineteen others died of the disease or committed suicide. One died of apoplexy one year after treatment, and one of "heart trouble" three months after treatment. The one remaining patient is still under observation without evident recurrence. The summary of this group is shown in Table I.

TABLE I

THIRTY-FOUR INOPERABLE CASES TREATED BY RADIOTHERAPY

Cases	P. O. D.	Died of Disease	Died of Other Cause	Not Traced	Alive under 5 Years	Living over 5 Years
34	1	22	2	8	1	0

From the above analysis, it can readily be seen that, with but a few exceptions, the group was made up of unfavorable or hopeless cases for whom there were no expectations of obtaining a cure. For this reason, they cannot be considered as comparable to the cases usually reported by radiologists. Furthermore, it would be unfair to attempt to draw any conclusions as to the value of irradiation for such cases, as, in the absence of details as to dosage, *etc.*, in the older histories, it is impossible to say whether or not the treatment employed was adequate as judged by present standards. In this connection, it should be explained that it is only within the last five or six years that a well equipped radiotherapy department was established in this hospital under the Department of Surgery.

NINETY-EIGHT CASES TREATED BY SURGERY OR BY A COMBINATION OF SURGERY AND RADIOTHERAPY.—There were actually 103 cases in this group, but five of these have been excluded, as no pathologic report could be found. One of these is a five year survivor who had an ulcerated tongue lesion with indurated edges, 1½ x 1 cm. in size, and a negative Wassermann reaction. The tongue lesion was destroyed by the actual cautery without a biopsy being taken, and the cervical nodes after removal showed no metastases. The remaining 98 cases were all squamous cell carcinomata.

The following plan has been adhered to in compiling statistics:

Percentages of deaths, survivals, *etc.*, are computed upon the total number of cases operated upon, and not merely upon the cases traced.

Only cases which, from their histories, appear to be primary in the tongue, and those in which the clinical diagnosis was verified by a pathologic examination are included.

Cases that died while still in the hospital, following the operation upon the tongue or nodes, are classed as postoperative deaths.

A patient to be classed as a "five year survivor" must have lived free from disease for at least five years from the last operation, or, in the case of recurrence, from the time at which such recurrence was eradicated. Those that recurred or died subsequent to the five year period are entered among the five year survivors.

The term "primary" is used to designate a case which gives no history of previous treatment of the lesion before applying to the hospital for treatment.

The term "secondary" refers to cases in whom previous treatment, such as cauterization, radium treatment, or excision, did not eradicate the disease, or where recurrence followed their use. Patients treated by radium, either in the hospital or elsewhere, who had recurrences, later treated surgically, are grouped with the surgical cases.

In preparing statistical data, the writer has encountered the difficulties so often met with when an attempt is made to study hospital histories. Many of the older records were found to be incomplete, and even among the more recent ones there is frequent omission of information on important points. It has been impossible to obtain complete data from all the histories along any one line of investigation. As a result, the total number of cases upon which statistics are based vary in almost every instance.

ETIOLOGIC FACTORS.—*Age.*—Sixty-one per cent of the patients were between 50 and 69 years of age, the number being about equally distributed between the fifth and sixth decades. The average age for the entire group is 58.1 years, which is about four years higher than the average given in Lane-Claypon's[2] analysis of the literature. The oldest patient was 79 years old, and the youngest was a man of 31.

TABLE II

AGE DISTRIBUTION OF NINETY-SEVEN CASES*

25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–80	Over 80
0	3	7	6	9	15	13	20	11	5	8	0

* Age not given one case.

While a few cases of carcinoma of the tongue have been reported as occurring in children, the youngest on record seems to be a small papillary squamous cell carcinoma in a newborn infant recently reported by Frank, Enfield and Miller.[3]

Sex.—There are 14 women in this series, giving a ratio of about one woman to seven men (14 per cent), which is above the average of 9.8 per cent obtained by Lane-Claypon from the statistics of a large number of observers.

Heredity.—Out of 80 of the 98 cases in which the family history is mentioned, only five (6 per cent) give a family history of cancer, which is not of much significance.

Tobacco.—In 76 histories where the use of tobacco is referred to 13 (17 per cent) denied its use, 27 (36 per cent) used it in moderation, and 35 (46 per cent) indulged to excess; in one the amount used is not mentioned. Seventeen (22 per cent) smoked a pipe, and one (1 per cent) chewed tobacco in addition to smoking.

Alcohol.—In this series the use of alcohol, when mentioned in the histories, was found to be too indefinite to warrent tabulating.

Dental Condition.—In 65 histories in which the condition of the teeth is recorded, the teeth in 41 (63 per cent) are described as "bad," "poor," or "irritating." An additional 12 (18 per cent) were wearing plates following removal of poor teeth, and in but 12 (18 per cent) were the teeth described as "good" or "fair." Six patients definitely attributed the tongue lesion to irritation from rough teeth, four to injury from poorly fitting plates or bridgework, one to biting his tongue, and one to injury by a dentist's emery wheel.

Syphilis.—In 27 histories there was no reference to the presence or absence of syphilis. Of the remaining 71 cases, a syphilitic history, or a record of antisyphilitic treatment, or a positive Wassermann reaction was noted in 19. This gives an incidence of 27 per cent among the 71 cases in whom the presence or absence of syphilis was noted, or an incidence of 19 per cent for the entire group. The true figures probably lie between 19 and 27 per cent. That syphilis is a very definite etiologic factor in tongue cancer seems without question from the following statistics. Belote,[4] from the University Hospital of Ann Arbor, found a seropositive syphilitic reaction in 29.3 per cent of 92 cases of cancer of the tongue, distributed as follows: 5.8 per cent among women, and 34.7 per cent among men. According to Fraser[5] in tongue cancer the syphilitic proportion is 42.3 per cent, and when the malignant lesion affects the dorsum of the tongue the syphilitic incidence rises to 78.3 per cent. Others give higher figures, as Fournier,[6] who found out of 184 tongue cancers evidence of syphilis in 155 (84 per cent). Fournier's cases, however, were taken from patients who were mostly syphilitic. At the other extreme may be mentioned Lund,[7] who found evidence of syphilis in only 17 per cent of 401 tongue cancers; but he also found that of all mouth cancers the highest incidence of syphilis was present in cancer of the tongue.

The association of syphilis with tongue cancer has a marked influence on the prognosis. Lund found that patients in whom syphilis and cancer of the tongue were both present showed a greater proportion of highly malignant tumors than did patients without syphilis. In this group of cases this could not be verified, for the patients with positive Wassermanns were equally divided between the Grade 1 and 2 tumors, and in all of the few Grade 3 cases the Wassermann reaction was either negative or not stated. The results, however, in the cases operated upon with positive Wassermanns were almost invariably fatal. Out of 13 such cases, there were five postoperative deaths, and of the eight remaining six died within 15 months, one within three years, and one is untraced. Thus, of the total number of cases with positive Wassermanns operated upon, 92 per cent are known to be dead. MacGregor,[8] from a study of 25 cases in which there was malignancy of the tongue on a luetic base, expresses the opinion that it is difficult to think of anything but a fatal prognosis where a combination of progressive malignancy of the tongue is present in a syphilitic subject. Meland[9] in a series of 95 intra-oral cancers reports no recoveries among seven cases with a history of syphilis. Lund, out of 40 tongue cases with evidence of syphilis, mentioned one cure (2.5 per cent). Results from radium treatment of tongue cancer complicated by syphilis are, likewise, unsatisfactory, and extensive sloughing of the tissues is not uncommon even though the dose is not excessive.

Leukoplakia.—Leukoplakia was noted in five cases (5 per cent). This is an unusually low percentage for tongue cancer associated with leukoplakia. In only one of the five cases (20 per cent) was there an associated syphilitic history. Belote states that leukoplakia is found in 20 per cent of the seronegative cases and was found about twice as frequently in seropositive cases of tongue cancer. Lund gives 20 per cent as the proportion of all cases of leukoplakia that show syphilis. Fraser found that the incidence of leukoplakia in dorsal tongue cancer was especially high, *i.e.,* 90 per cent of the cases being preceded by leukoplakia.

THE LOCAL LESION.—*Alleged Duration of the Lesion before Admission to the Hospital.*—Discarding recurrent or secondary cases previously treated elsewhere, there are 70 histories in which the patients describe the duration as shown in Table III.

TABLE III

DURATION OF LESION IN 70 CASES

Months	Cases	Years	Cases
Under 3	17 (24.3 per cent)	1–2	10 (14.3 per cent)
3–6	25 (35.7 per cent)	2–3	5 (7.1 per cent)
6–12	11 (15.7 per cent)	3–5	2 (2.8 per cent)

The accuracy of the patient's observation as to duration is open to considerable question in a number of the histories, especially where the lesion was described as being present for a number of years. Some of these were probably benign lesions, the change to malignancy not being recognized by the patient. On the other hand, some lesions described as of very short duration were advanced cancers. It is possible, therefore, that these inaccuracies in the two extremes balance one another. Based on the above statistics, the average duration of the lesion before the patient presented himself for treatment was 7.4 months, close to half the average, natural duration for cancer of the tongue, which is placed by Greenwood (quoted by Lane-Claypon) at 16.4 months. In examining these cases, it was found that private patients came for relief only a little sooner than did the clinic cases. While 60 per cent of the cases presented themselves for treatment with a history of having had the lesion less than six months, approximately 62 per cent of these were private and 57 per cent clinic patients.

For cases that showed cervical metastases, the average length of time the patient had the lesion before applying for treatment was 6.1 months. Raven[10] states that node involvement in tongue cancer occurs in 69 per cent of the cases before six months, 42 per cent before three months, and in 27 per cent before two months. Simmons[11] in a group of intra-oral cancer found that 6.6 months was the average duration before treatment in cases with involved nodes.

Location of Lesion.—In 92 histories the sites given of the location of the lesion are shown in Table IV.

TABLE IV

LOCATION OF LESION IN 92 CASES

Tip	4 (4.3 per cent)
Margin, anterior ⅔	40 (43.5 per cent)
posterior ⅓	15 (16.3 per cent)
Dorsum	13 (14.1 per cent)
Base	5 (5.4 per cent)
Under surface	10 (10.8 per cent)
Whole tongue	5 (5.4 per cent)

Size of Lesion.—Classification under size is made difficult from the lack of uniformity in the descriptive terms employed. At times the lesion is described as small, medium, or extensive, and in other instances its actual size in centimeters or inches is given. Classifying as small all lesions of 1 cm. or under, as medium those between 1 and 2 cm., and as extensive those over 2 cm. and those that have spread beyond the tongue to other parts of the oral cavity, the following figures were obtained in 83 cases where the lesion was described (Table V).

TABLE V

SIZE OF LESION IN 83 CASES

0–1 cm. (small)	13 (15.6 per cent)
1–2 cm. (medium)	17 (20.5 per cent)
Over 2 cm. (extensive)	53 (63.8 per cent)

Type of Growth.—In 83 cases the type of growth is shown as in Table VI.

TABLE VI

TYPE OF GROWTH IN 83 CASES

Papillomatous	9 (10.8 per cent)
Tumor	11 (13.2 per cent)
Ulcerative	63 (75.9 per cent)

The small percentage (10 per cent) of a relatively favorable type of growth (papillomatous) and the high percentage (75 per cent) of the more malignant ulcerative tumors is noteworthy.

Grading of the Tumor.—Ninety-two of the 98 cases are graded according to Broder's classification. There were 50 (54 per cent) Grade 1, 38 (41 per cent) Grade 2, four (4 per cent) Grade 3, and no Grade 4 tumors.

Comparison of groups of cases each graded by different pathologists is not of great value, as there may be considerable variation through a difference of interpretation of the microscopic picture. This fact is well illustrated when the figures in this series and those given by Meland are compared with those of other observers. In this series there are 95 per cent Grade 1 and 2 and only 4 per cent Grade 3 tumors. Meland's figures based on 47 tongue cases, of which 19 are graded, are somewhat similar: five (twenty-six per cent) Grade 1, 12 (sixty-three per cent) Grade 2, one (five per cent) Grade 3, and one (5 per cent) Grade 4. Others report a much higher percentage of Grade 3 and 4 tumors. Pfahler and Vastine,[12] in 186 tongue cases treated by radiotherapy, found 53 per cent Grade 3 and 4. Berven,[13] from his tongue cancers, reports 46.15 per cent Grade 3 and 5.12 per cent Grade 4 tumors. Judd and Phillips,[14] from the Mayo Clinic, found more than 50 per cent of tongue cancers were Grade 3 and 4 (Broders). Blair, Brown, and Womack[15] found that out of 33 tongue cases the Grade 3 and 4 tumors each formed 33 per cent of the total.

The grading of the primary growth, as will be shown later, did not have much influence on the prognosis. Furthermore, it did not prove of great value as a guide to the presence or absence of metastases, as shown in Table VII.

CONDITION OF THE NODES.—Of the 98 cases, 59 showed palpable nodes on admission, 22 (38 per cent) of which were bilateral. In 23 histories it is stated

TABLE VII

INCIDENCE OF METASTASES IN RELATION TO GRADE OF TUMOR

	Cases	Nodes Not Involved	Nodes Involved
Grade 1	36	19 (52.8 per cent)	17 (47.2 per cent)
Grade 2	33	16 (48.5 per cent)	17 (51.5 per cent)
Grade 3	4	3 (75 per cent)	1 (25 per cent)

there were no palpable nodes, and in 16 instances no mention is made of their presence or absence. Out of 80 cases in which nodes were operated upon and examined microscopically, 38 (47 per cent) showed metastases. Of 48 cases *with palpable nodes* which were examined microscopically, 23 (48 per cent) showed no metastases; of 18 cases where it was stated *no nodes were palpable,* seven (39 per cent) showed metastases; and out of 14 cases where the *nodes were not mentioned,* six (42 per cent) showed metastases. In other words, one-half of those with palpable nodes and over one-third of the cases without palpable nodes, or where the presence or absence of nodes was not mentioned, showed involvement on microscopic examination.

Phillips,[16] in a series of 319 *buccal* carcinomata, reports that out of 59 with clinical metastases, 22 (37.3 per cent) were negative microscopically, and of 31 cases with no clinical metastases, 16 (51.6 per cent) showed carcinoma on microscopic examination. In a group of *oral* cancers, Simmons[17] found that out of 22 cases with clinically palpable nodes, ten (45 per cent) showed no cancer, and of 20 cases of nonpalpable nodes, seven (34 per cent) proved to be cancerous. It is thus evident that the usual classification of the condition of the nodes, into clinically palpable and clinically nonpalpable, is not a reliable index of the presence or absence of metastases. As a more accurate method, Lund and Holton[18] suggest the division of the nodes into "small" and "large" nodes. Under "small" nodes they include the following: cases described as small, not enlarged, negative, up to 1 cm. in size, or not mentioned. All others they include in the large node group. Reclassifying Simmons' cases into these groups, they found that about the same number of cases with small nodes showed metastases as were negative, while 100 per cent of the cases classed as "large" nodes proved to be metastases.

RESULTS OF TREATMENT.—Of the 98 cases upon which the foregoing study is based, 88 were treated by surgery and ten by a combination of radiotherapy and surgery. Seventy-three were treated prior to 1931 and 25 since that time. Included among the total treated are 25 private patients, and the writer is greatly indebted to Drs. George H. Semken, Franz J. A. Torek, Henry H. M. Lyle, Joseph E. King, Robert H. Kennedy, and William F. MacFee for permission to include them in this study. The 73 clinic cases were treated by more than 15 different surgeons as well as their assistants, so that the results can be considered as representing the work of a fairly large hospital group. A summary of the cases treated with division into two groups, prior to 1931 and since 1931, follows. In Tables VIII and IX are included all cases operated upon, whether primary or secondary, with and without metastases, and those upon whom palliative operations only were performed.

TABLE VIII

GROUP OPERATED UPON BETWEEN 1917 AND 1930

Postoperative deaths	22 (30.1 per cent)
Recurred and lost, or died from recurrence or with disease	30 (41 per cent)
Died from other causes	1 (1.4 per cent)
Untraced	5 (6.8 per cent)
Surviving five years or more	15 (20.5 per cent)
Total cases	73

TABLE IX

GROUP OPERATED UPON BETWEEN 1931 AND 1935

Postoperative deaths	4 (16 per cent)
Recurred and lost, or died from recurrence or with disease	7 (28 per cent)
Died from other causes	1 (4 per cent)
Untraced	1 (4 per cent)
Surviving less than five years	12 (48 per cent)
Total cases	25

ANALYSIS OF CASES OPERATED UPON BETWEEN 1917 AND 1930.—The 1917-1930 group only is used as a basis for computing "cures," the results from various types of operation, *etc.* Seventy of these cases were treated by surgery and three by a combination of radiotherapy and surgery. In 42 of the 73 cases, the disease was limited to the tongue; in 14 it had involved also the floor of the mouth; in five, the tonsil; in three, the tonsil as well as the floor; in two, the superior portion of the larynx; and in two, the lower jaw. The other five could not be classified on account of poor histories. Thus, in 26 out of the 73 cases (36 per cent), the disease had already spread locally beyond the tongue. Also in 20 of the 42 cases (48 per cent) in which the disease was limited to the tongue, metastases were found in the cervical nodes at operation. We find, therefore, that almost two-thirds of the cases could be classified as well advanced. Also among the above were 17 cases that still had the disease, or were definite recurrences following some form of previous treatment, such as cauterization, radiotherapy, or an incomplete operation.

Cases Treated by Surgery.—In the surgically treated cases, the tongue lesion was removed by surgical dissection as a rule; in other instances the actual cautery, electrocoagulation, or the electrocautery was employed. An intra-oral operation was performed in 42 instances, after division of the lower jaw in 11 cases, and through the neck in nine instances, and once after division of the cheek. For the removal of the cervical nodes the upper cervical node dissection as described by Dr. George H. Semken[19] was employed in most of the cases. Briefly, this consists of a block dissection of the submental, submaxillary, parotid, carotid, and posterior carvical nodes to below the level of the omohyoid crossing, together with the platysma and all fatty tissue, the submaxillary gland, and the lower pole of the parotid gland. Unless involved, the internal jugular vein and the sternomastoid muscle are not removed. In some cases, notably where a bilateral node dissection was performed in one stage, a variation of this standard upper node dissection was used. As modified, the operative field did not extend as low or as far posteriorly as in the typical neck operation. In eight instances, it is recorded that the upper node operation was supplemented by a supraclavicular node dissection on the affected side. In two of these, the supraclavicular operation was bilateral. Our present procedure for treatment of the nodes, if the patient is in good physical condition, is preferably a complete bilateral node dissection down to the clavicle.

Postoperative radiation of the cervical region has not been employed as a routine. It appears to have been used in but 13 cases, none of whom have survived five years. Our feeling is that it is not of advantage to employ it. In the first place, if the removal of the cervical nodes is thorough, it is not necessary; in the second place, if recurrence takes place, the patient has a better prospect of obtaining some benefit from radiation if it has not been employed previously.

Results According to the Type of Operation.—There were six variations of operative procedure applied to the 70 cases treated by surgery:

(1) Simple excision of the tongue lesion (a questionable procedure for any tongue cancer, except as a palliative measure).

(2) Excision of the tongue and nodes of the opposite side of the neck in one stage, and excision of the nodes of the affected side at a later date. This is the ideal method of dealing with cases in good physical condition and with tongue lesions not requiring too extensive an operative procedure.

(3) Excision of the tongue and nodes of one or both sides, each in a separate stage. This type is, thus, either a two or three stage procedure. It is used principally in cases where the tongue lesion requires so extensive an operation that to add a neck dissection, as in procedure 2 above, would be more than the patient could withstand with safety.

(4) Excision of bilateral nodes in one stage and the tongue lesion at a later stage.

(5) Excision of the tongue and the nodes of the affected side at one operation.

(6) Excision of the tongue and a bilateral node operation in one stage.

The last three procedures, on account of the high operative mortality attending them, have not been employed since 1929.

For the purpose of drawing conclusions as to the relative risk, percentage of cures, *etc.*, from these operations, they are tabulated in detail in Table X, and are divided into complete and incomplete operations. In the latter group are placed a number of operations which from the history and preoperative findings obviously required more thorough surgery than was actually accomplished, the operation not being completed, either because the patient did not survive the first stage of the operation, or else refused further treatment, or because the condition was found to be inoperable.

The two cases in which excision of the primary lesion only was performed had small papillary tumors, showing early malignant changes, for which local excision was evidently considered sufficient. One was followed

TABLE X

SUMMARY OF 70 CASES TREATED SURGICALLY BETWEEN 1917 AND 1930

Type of Operation	Cases	P. O. D.	Recurred and Lost, or Died	Died Other Causes	Not Traced	Five Year Survivals
Excision of tongue lesion only.....	2	0	1 (50 per cent)	0	1 (50 per cent)	0
Excision of tongue and nodes of opposite side, one stage, nodes of same side later.	13	3 (23.1 per cent)	3 (23.1 per cent)	0	0	7 (53.8 per cent)
Complete......	11	1 (9.1 per cent)	3 (27.2 per cent)	0	0	7 (63.7 per cent)
Incomplete....	2	2 (100 per cent)	0	0	0	0
Tongue and nodes each operated upon in a separate stage (a two or three stage operation).....	19	6 (31.5 per cent)	7 (36.8 per cent)	1 (5.3 per cent)	3 (15.8 per cent)	2 (10.6 per cent)
Complete......	13	1 (7.7 per cent)	6 (46.1 per cent)	1 (7.7 per cent)	3 (23.1 per cent)	2 (15.4 per cent)
Incomplete....	6	5 (83.3 per cent)	1 (16.6 per cent)	0	0	0
Bilateral nodes first stage, tongue later...	11	3 (27.2 per cent)	7 (63.6 per cent)	0	0	1 (9.1 per cent)
Complete......	9	1 (11.1 per cent)	7 (77.7 per cent)	0	0	1 (11.1 per cent)
Incomplete....	2	2 (100 per cent)	0	0	0	0
Tongue and nodes of same side in one stage......	16	7 (43.7 per cent)	6 (37.4 per cent)	0	0	3 (18.7 per cent)
Tongue and bilateral nodes in one stage..........	6	3 (50 per cent)	2 (33.3 per cent)	0	0	1 (16.6 per cent)
Palliative operations..........	3	0	2 (66.6 per cent)	0	1 (33.3 per cent)	0
Totals......	70	22 (31.4 per cent)	28 (40 per cent)	1 (1.4 per cent)	5 (7.1 per cent)	14 (20 per cent)

for over two years without recurrence and was then lost. Another had a local recurrence in two years which was excised, and returned with a second recurrence four years later, and was then lost track of.

Exclusive of the above group, the lowest operative mortality occurs in the three groups where the operations on the tongue and the nodes of the same side were performed in separate stages. In these groups the operative mortality ranges from 23.1 to 31.5 per cent for the combined "completed" and "incompleted" cases, and from 7.7 to 11.1 per cent in the completed cases. In the two groups where the tongue and nodes of the affected side of the neck were operated upon at the same time, the mortality ranges from 43.7 to 50 per cent. The lesson this teaches is that when the operation is performed in such a way as to leave a communication between the mouth and the freshly opened cellular spaces of the neck, the operative risk is enormously increased. Fraser gives 8.3 per cent as the mortality of the stage operations against 52.6 per cent mortality for the simultaneous mouth and neck operation. Blair and Brown[20] give a 34 per cent mortality for the combined neck and tongue operation. Fischel[21] states that the results in tongue cases were poor, both as to postoperative deaths and cures, when the intra-oral and neck dissections were combined; but where the neck operation was performed two weeks later the mortality was low.

Under palliative operations, three cases are included. One patient, after a cervical node operation had been done, was deemed to be inoperable, and the tongue lesion was not removed. He received some postoperative radiation and died in six months. Another refused to have the cervical nodes removed after excision of the tongue lesion and died in seven months. The third, a man of 69, with bilateral palpable cervical nodes, had his tongue lesion first removed by the cautery and four months later by surgical excision, and was then lost track of. It is probable that some of the cases placed in the incomplete group, where the tongue and nodes were removed separately, belong among these palliative operations, but, on account of the lack of details in their histories, they have not been included among the latter.

Cases Treated by Combined Radiotherapy and Surgery.—A summary of three cases so treated is given in Table XI.

TABLE XI

SUMMARY OF CASES TREATED BY COMBINED RADIOTHERAPY AND SURGERY, 1917–1930

	Cases	P. O. D.	Recurred and Lost, or Died	Died Other Causes	Not Traced	Five Year Survivals
Radium to tongue, node operation later.....	1	0	0	0	0	1 (100 per cent)
Palliative operations and radium.....	2	0	2 (100 per cent)	0	0	0
Total.........	3	0	2 (66.6 per cent)	0	0	1 (33.3 per cent)

The one case whose tongue lesion was treated by implantation of radium followed by a unilateral node dissection is a seven year survival. The nodes on examination were found to be carcinomatous. The other two were inoperable and are classed under palliative operations. In one, the external carotid artery was ligated and part of the tongue was removed, followed by implantation of radium. The other was given external radiation and both lingual arteries were tied. One died within three months, and the other within ten months. The results in this group, with 33.3 per cent five year survivals, are better than those obtained from surgery alone, but the cases are too few to warrant drawing definite conclusions.

Results Where (1) the Tongue Operation Preceded, or (2) Followed the Node Operation, and Where (3) There was a Simultaneous Tongue and Node Operation.—In order that the "tongue first" group and the "node first" group may be comparable to the simultaneous tongue and node group, cases that died from the first stage of operations where the tongue or nodes were removed first are omitted (Table XII).

The best results, both as to five year survivals and recurrences, were obtained where the tongue operation preceded that on the nodes of the affected side, and the worst results are seen in the group in which the nodes of the affected side were removed first. In spite of this, removal of the nodes first may be necessary in cases of rapidly developing lymphatic involvement, where

TABLE XII

SUMMARY OF CASES OF (1) TONGUE REMOVAL FIRST, (2) NODE REMOVAL FIRST, AND (3) SIMULTANEOUS REMOVAL OF TONGUE AND NODES

	Cases	P. O. D.	Recurred and Lost, or Died	Died Other Causes	Not Traced	Five Year Survivals
Tongue operation first, followed by node operation later..........	15	1 (6.7 per cent)	5 (33.3 per cent)	1 (6.7 per cent)	0	8 (53.3 per cent)
Node operation first, tongue operation later...	18	1 (5.5 per cent)	12 (66.6 per cent)	0	3 (16.6 per cent)	2 (11 per cent)
Simultaneous tongue and node operation......	22	10 (45.4 per cent)	8 (36.3 per cent)	0	0	4 (18.2 per cent)

the delay caused by operating upon the tongue first might result in the nodes becoming inoperable. The simultaneous tongue and node operation, while giving better results as to five year survivals and recurrences than the node first group, had a mortality rate of 45.4 per cent. Fraser, in his series of *mouth and tongue cancer,* states that he obtained his best results as to recurrences in a simultaneous tongue and node operation. His results were about the same whether the tongue or nodes were removed first.

Results According to the Completeness of Removal of the Cervical Nodes.—The nodes of the affected side only were excised in 36 instances, while a bilateral node operation was performed on 27 cases. The percentage of five year survivals from the bilateral node operation is more than double that obtained when the unilateral operation only was performed, while the percentage of recurrences and deaths after leaving the hospital is about the same whether a bilateral or unilateral operation was performed (Table XIII). The high postoperative death rate from the unilateral node operation is misleading in that it would appear to be a more dangerous procedure than a bilateral operation. This high percentage (40.7 per cent) is due to the fact that seven of the 11 deaths from the unilateral node operation occurred in cases where the tongue and nodes of the same side were operated upon at one sitting.

The results where a unilateral or bilateral node dissection was supplemented by a supraclavicular node operation are even better than in the other two groups, with 50 per cent five year survivals. The fact that there were no deaths from this procedure is noteworthy, but it should be stated in three of the eight cases, the supraclavicular dissection was performed in a separate stage from the upper node dissection. Prior to 1931, the supraclavicular node operation was performed in only eight (12 per cent) of the 63 neck dissections. Since that time, it has been employed in seven (58 per cent) out of 12 neck operations.

Postoperative Deaths.—There were 26 postoperative deaths among the 98 cases, giving a mortality rate of 26.1 per cent for all cases, and 28.4 per cent for those treated solely by surgery. No cause is assigned for 14 of the deaths. Of the remaining 12, five died from pneumonia, two from pulmonary

TABLE XIII

RESULTS ACCORDING TO THE COMPLETENESS OF CERVICAL NODE OPERATION

	Cases	P. O. D.	Recurred and Lost, or Died	Died Other Causes	Not Traced	Five Year Survivals
Unilateral node operations	27*	11 (40.7 per cent)	10 (37.7 per cent)	0	2 (7.4 per cent)	4 (14.8 per cent)
Bilateral node operations.......	36	7 (19.4 per cent)	16 (44.4 per cent)	1 (2.8 per cent)	1 (2.8 per cent)	11 (30.5 per cent)
Complete node operations on the affected side	8†	0	4 (50 per cent)	0	0	4 (50 per cent)

* One case in whom the tongue was treated by radium and the nodes were removed is included.

† All of these cases, of course, are from among the above groups in which the nodes of one or both sides were removed.

edema, one from lung abscess, one from infection, one from shock, one from hemorrhage, and one from suffocation.

The 28.4 per cent operative mortality for the entire group of 88 cases treated by surgery alone is high compared with the statistics on similar cases from other clinics. Butlin[22] in 197 operations had only a 10 per cent mortality; Hartmann[23] reports 10 per cent mortality. Blair, Brown, and Womack had an operative mortality of 26.9 per cent from their tongue operations. Fischel[24] in 59 cases had a 20 per cent mortality. Moure and Martin[25] out of 65 cases lost 16 (24.6 per cent) postoperatively. Some other figures are lower, but, for combined early and late cases, the postoperative mortality probably ranges around 20 per cent.

The large number of fatalities in the simultaneous operations on the tongue and nodes of the same side, with its 45.4 per cent mortality rate, partly accounts for these high percentages. Since the year 1929, no one stage operations on the tongue and nodes of the same side and no bilateral node operations in one stage have been performed, and the postoperative death rate among the surgical cases for the five year period since then (1931–1935) is 16.7 per cent. In the 14 year period prior to this (1917–1930), the postoperative death rate was 31.4 per cent, showing an improvement of almost 50 per cent in results since operative methods with a recognized high mortality rate were abandoned. Another factor that may have a bearing on the high postoperative death rate is the age of some of these cases. While six of the 26 deaths were in patients 50 years of age or under, the average age of the remaining 20 was 63.4 years. The ages of six of the latter ranged between 68 and 79 years. Applying our present principles of treatment to the above group, we probably would not treat by surgery these old patients with extensive lesions requiring very radical operations for complete removal. For such cases, radiotherapy would offer a better chance for prolongation of life and possibly control of the disease to such an extent that the patient could pass his few remaining years in comparative comfort.

Recurrences and Deaths after Discharge from Hospital.—Thirty of the 73 cases (41 per cent) recurred or died after discharge from the hospital.

Twelve (40 per cent) of these had involvement of the nodes when operated upon. On the charts of 11 patients, it is stated merely that they died, and on three that they died from the disease. Sixteen others recurred and either died, commited suicide, or were lost. Five of these recurrences were local, four were in the lymph nodes, and in three the recurrence was both local and in the neck. In the remaining four histories, it is simply stated that there was a recurrence. All but two of the 16 recurrences (87 per cent) took place within the first year following the operation. There were, in addition, two local recurrences and one case of cervical metastases which are not entered in the recurrence column as they are among the five year survivals. The two local recurrences after further surgical treatment are still alive and free from disease over five years. The case of cervical metastases, after remaining well and free from disease nine years, developed supraclavicular nodes and died a year later.

Examination of the neck recurrences revealed three cases of cervical metastases, without local recurrence, in which at the original upper node operation the pathologic examination showed only hyperplasia of the nodes. In two of the cases, the metastases occurred in the superclavicular region of the affected side (one nine years after operation); in the third, in the supraclavicular region of the opposite side. A fourth case showed, three months after removal of hyperplastic nodes from one side, involvement of the nodes of the opposite side and recurrence below the end of the horizontal incision on the side originally operated upon. As there were 36 cases of hyperplastic nodes operated upon, over 10 per cent of them developed metastases either on the same side below the limits of the original neck dissection or upon the opposite side without the upper cervical nodes showing involvement. In other words, there was an error of around 10 per cent in the pathologic diagnosis due to the impossibility of examining every portion of the specimen. Brown[26] found that out of 140 neck dissections for carcinoma of the mouth, there were 13 instances where the pathologic report of the absence of cancer did not coincide with the clinical course. Among his cases, the longest period that carcinoma lay dormant in the nodes was seven years.

These cases serve as an argument for the complete removal of the lymph nodes to the clavicle from both sides of the neck where the condition of the patient will permit. While certain areas of the tongue are drained by definite groups of lymphatics, it is well recognized that metastases from tongue cancer may follow peculiar courses, not infrequently showing in the deep carotid nodes, or in those immediately above the clavicle, as for example, when the anterior portion is involved, without there being involvement of the superficial groups. More rarely, metastases occur first upon the side of the neck opposite to that upon which the lesion is situated.

Died from Other Causes.—The one case in this group died a short time after operation, free from disease, from erosion of the carotid artery, the result of destruction of the thin neck flap by postoperative roentgen therapy.

Cases Not Traced.—When this work was begun, the fate of many cases was unknown, and it seemed an almost impossible task to hope to obtain data on some of the older ones. However, through the excellent work done by the Social Service Department, the results in all but five of the 1917–1930 group are now known. One of these had cervical metastases when operated upon, so it can be safely assumed that he had died. Up to the present time, information as to what happened to the other four is entirely lacking.

Survivals of Five Years and Over.—There are 15 five year survivals (20.5 per cent) from all operations, or 20 per cent for all types of cases treated by surgery alone. The distribution of the survivors is shown in Table XIV.

TABLE XIV

DISTRIBUTION OF THE SURVIVING CASES

5 to 6 years	3 cases
6 to 7 years	1 case
7 to 8 years	2 cases
8 to 9 years	1 case
9 to 10 years	4 cases
Over 10 years	4 cases

Two of the above have since died. One, after nine years of freedom, developed supraclavicular metastases. The other died of a "heart attack" after seven years.

The results as to five year survivals among the private cases were very much better than among the clinic patients. There were 36.4 per cent five year survivals in the former group and 13.7 per cent in the latter. It might be assumed that these better results were due to the fact that private patients had earlier lesions. This is not the case, however, for, as already shown, among the cases that presented themselves for treatment with lesions of under six months' duration, there were only 5 per cent more private patients than clinic patients, while out of the cases that showed cervical metastases, 36 per cent were private and 35 per cent clinic cases. The explanation probably is that the private patients were in better physical condition for extensive operations and came under the care of more skilled operators. Furthermore, none of the cases in which syphilis was present occurred among the private patients.

Results as to five year survivals considered from the standpoint of whether the case was primary or secondary, and whether the cervical nodes

TABLE XV

RESULTS IN PRIMARY AND SECONDARY CASES WITH AND WITHOUT METASTASES

	Cases	Five Year Survivals
Primary cases, nodes not involved	30	10 (33.3 per cent)
Secondary cases, nodes not involved	7	2 (28.5 per cent)
All cases, nodes not involved	37	12 (32.4 per cent)
Primary cases, nodes involved	22	2 (9.1 per cent)
Secondary cases, nodes involved	4	1 (25 per cent)
All cases, nodes involved	26	3 (11.5 per cent)

were uninvolved or involved are shown in 63 cases in which the nodes were subjected to pathologic examination (Table XV).

From the above, whether the case was primary or secondary seems to have little bearing on the result. In fact, the results were a little better in the secondary cases with 27 per cent five year survivals against 23 per cent in the primary cases. *Of prime prognostic importance is the presence or absence of cervical metastases.* Without metastases, there were 32.4 per cent five year survivals; while with metastases, the five year survivals fell to 11.5 per cent. Likewise, the size and the grade of the tumor had little prognostic value when the primary lesion was treated surgically (Tables XVI and XVII).

TABLE XVI

RESULTS ACCORDING TO THE SIZE OF THE LESION

Size	Cases	Five Year Survivals
Small (0–1 cm.)	11	2 (18.1 per cent)
Medium (1–2 cm.)	11	2 (18.1 per cent)
Large (2 cm. and over)	37	6 (16.2 per cent)

TABLE XVII

RESULTS ACCORDING TO THE GRADE OF THE TUMOR

Grade	Cases	Five Year Survivals
1	40	8 (20 per cent)
2	28	4 (14.3 per cent)
3	2	1 (50 per cent)
4	0	0

There have been many excellent papers on the results of the treatment of tongue cancer published during the last five years, but in many cases it has been impossible to use the statistics on account of the manner in which the material was presented or from the fact that survivals of from under one year upward were sometimes included with the five year survivals in computing the results. From some of these reports the writer has attempted to figure out the five year survivals, but, in each instance, it is indicated when such percentages are used. From clinics where surgery was mainly employed the result are as follows: From the Barnard Free Skin and Cancer Hospital, 1906–1925, Fischel reports three (5 per cent) out of 59 cases as living and well five years (this group includes all types of cases). Gask's[27] statistics from St. Bartholomew's Hospital show 17.1 per cent five year survivals. Moure and Martin, in 57 cases of histologically confirmed cancer of the tongue, had 12 five year cures (apparently all types of cases are included, and there are also included some cases treated during the last five years, so that the actual percentage of five years survivals cannot be determined). New and Figi,[28] from the Mayo Clinic, in 162 cases report 58 (37.2 per cent) five year survivals from all types of cases. Without metastases they had 50 per cent five year survivals and with metastases 14.3 per cent (these figures, however, are based on the cases traced and would be slightly lower if based on all the cases treated). Patterson[29] reports 28 cases of microscopically verified tongue cancer, operated upon by diathermy with seven (25 per cent) survivals of over five years. Of these, 13 had cervical metastases, with no five year survivals, and without metastases there were 49 per cent five year survivals. From the Collis P. Huntington Memorial Hospital and the Massachusetts General Hospital, from 1918 to 1924, from a series of 763 oral cancers, Simmons reports, in 42 primary cases of tongue carcinoma without evidence of lymphatic metastases, 12 (29 per cent) five year "cures."

Among those using radiation alone, or as the principal form of treatment, for the tongue lesion, the method of treating the cervical nodes varies considerably. In the majority of clinics, nonpalpable nodes are treated by external radiation or the radium collar. Palpable nodes in some clinics are treated by external radiation or radium, and a block dissection if they do not disappear. Others use either a block dissection for operable nodes, followed by the radium collar if the nodes are involved, or interstitial radium implants in the involved nodes. Results from some of the clinics where the above methods are used are as follows: Cade,[30] from the Westminster Hospital, reports from 18 tongue cancers two (11 per cent) five year survivals. He further states that of these 18, 13 had palpable nodes, seven of which were inoperable. Quick,[31] from the Memorial Hospital, out of 473 cases reports 39 cases free from disease from five to 12 years (the percentage of five year survivals cannot be determined, as in the 473 cases are included patients treated less than five years previously). Regaud's[32] statistics show the five year survivals for different portions of the tongue. Combining these figures, there were 58 (17.6 per cent) five year survivals from 330 cases of all types. From the Radiumhemmet in Stockholm, Berven reports separately for the purpose of comparison, for the years 1916 to 1921 and from 1922 to 1926. Combining his figures, on 104 cases from 1916 to 1926, there were 33 (32 per cent) five year "cures" for all cases. These were distributed as follows: Group 1 (without metastases), 60 cases with 32 (50 per cent) five year "cures." Groups 2 and 3 (with operable and inoperable metastases), 44 cases and one (2 per cent) five year "cure."

Berven's[33] later figures, for 1916 to 1928, give in 141 cases of tongue cancer 40 (28 per cent) five year "cures." From the Curie Foundation Roux-Berger,[34] in a series of 386 tongue cancers, reports the results separately for different portions of the tongue. Combining his figures, there were out of 382 microscopically verified cancers 18 per cent five year "cures." These were distributed according to their extent as follows: Under 2 cm., 55 cases with 25 (45 per cent) five year "cures." Over 2 cm., 327 cases with 46 (14 per cent) five year "cures." From the Liége University, Delrez and Desaive[35] give results in 52 tongue cancers for periods from six months to eight years. In this series there were five five year survivals. Pfahler[36] reports 16 (26.2 per cent) five year survivals.

Analysis of Cases Operated Upon Between 1931 and 1935.—In the group of 25 cases treated since 1930, there were four postoperative deaths, two of which occurred following palliative operations for extensive tongue lesions. In the 18 cases treated surgically, a stage operation was performed in all in which the tongue and nodes were operated upon, and it is noteworthy that the postoperative death rate is 16.7 per cent, an improvement of nearly 50 per cent over the mortality rate in the earlier group.

Of the seven cases that recurred, or died with the disease, one was treated surgically. This latter case, after a node operation had been performed, was felt to be inoperable, and the tongue lesion was not removed. The patient died from the disease in three months. The other six cases were from a group of seven in which the tongue lesion was treated by implantations of radium. In none of the six was there a permanent disappearance of the lesion. The seventh case, a Grade 3 tumor, is of too recent a date to determine the result. One of the seven cases was not graded, five had Grade 1 tumors, and one had a Grade 2 tumor. Four had positive Wassermanns and in three the lesion is described as extensive. All recurrences took place under two years. The results in these cases are very poor. Out of a total of 11 cases treated by a combination of radium and surgery (one patient, after recurrence, was treated by surgery and is now included among the surgical cases), there is but one patient whose tongue lesion remained free from disease after the use of radium. Reports from other sources show that a temporary disappearance of the lesion should be looked for in about 70 per cent of the cases, but that a certain number can be expected to recur. Fitzwilliams[37] states that a 75 per cent temporary result is obtained locally, and a 60 per cent permanent result. Cade, out of 169 tongue cases, reports the disappearance of the growth in 126 (74 per cent) and recurrence in 43 (25 per cent).

There are 12 cases (46 per cent) alive and free from disease less than five years. These are distributed as follows: One over three years, two over two years, one over one year, and eight under one year.

Summary.—(1) Ninety-eight cases of microscopically confirmed cancer of the tongue form the basis of this report.

(2) Two-thirds of the cases were advanced cancers in the sense of having spread beyond the limits of the tongue or showing node involvement. Eighty-eight were treated surgically, and ten by a combination of radium and surgery.

(3) Neither the size nor the grade of the tumor proved of much prognostic value among the cases treated surgically.

(4) Ninety-two per cent of the cases with positive Wassermanns operated upon died either postoperatively or within three years.

(5) The operative mortality for the entire group amounted to 26.1 per cent, and 28.4 per cent for those treated by surgery alone. In the last five years, the postoperative death rate was 16.7 per cent. The lowest mortality rate occurred where a "stage" operation was performed. Among the simultaneous tongue and node operations, the postoperative mortality ranges from 43 to 50 per cent.

(6) Twenty per cent of all cases treated by surgery survived five years or over. Without node involvement, there were 32.4 per cent five year survivals, and with node involvement 11.5 per cent five year survivals. Out of three cases treated by a combination of radium and surgery, there was one (33 per cent) five year survival.

(7) The best results as to five year survivals and recurrences were obtained where the tongue was removed first. The next best results followed a simultaneous tongue and node operation. The poorest results were obtained in those cases where the node operation preceded that upon the tongue.

(8) The results as to five year survivals are over twice as favorable from a bilateral node operation when compared to those obtained from an excision of the nodes of the affected side only, and they were even better when there was a complete node removal down to the clavicle.

(9) Five year survivals among the private patients were almost three times greater than among the clinic patients.

(10) Postoperative radiation was not used as a routine. There were not a sufficient number of cases in which it was employed to form any conclusion as to its value.

(11) In over ten per cent of the cases following removal of hyperplastic nodes by an upper node dissection, where there was no local recurrence, cervical metastases occurred later on the same side of the neck in the supraclavicular region or upon the opposite side of the neck.

(12) Among the cases treated by radium and surgery, the results as to the permanent eradication of the tongue lesion were very poor. Where radium was used for the primary lesion, a permanent disappearance of the cancer was effected in only ten per cent.

CONCLUSIONS

In the treatment of tongue cancer no one method should be used to the exclusion of others. Surgery and radium each have their place, and the selection of the form of treatment in individual cases must depend upon the condition of the patient, the extent and location of the primary lesion, and the radiosensitiveness of the tumor. While excellent results are reported by some radiologists from the routine treatment of the primary lesion by radium, our own preference, at the present time, is for a wide surgical removal of operable lesions, preferably by the diathermy knife. For very radiosensitive lesions, radium should be tried before resorting to surgery. Extensive lesions in the posterior part of the tongue often may be eradicated by electrocoagulation and the use of radium with less mutilation than where surgery alone is employed. Cases in which radium fails to cause a disappearance of the lesion should be treated surgically. Whether radium or surgery is employed in the treatment of the tongue lesion, it is felt that eradication of the primary lesion should be effected, as a general rule, before removal of the cervical nodes is attempted.

An objection to the surgical treatment of tongue cancer is the operative mortality. If operative procedures with a recognized high death rate are avoided and obviously poor surgical risks are refused operation, this should be well under 20 per cent for the combined tongue and node operation. That the use of radium is not unattended by some fatalities as the result of radium-necrosis, infection, and hemorrhage seems certain, but it is impossible to say just what the percentages are, as radiologists apparently do not list such cases as postoperative deaths.

When it comes to a question of the efficiency of surgery and radiation in the treatment of the cervical nodes, comparison of results from the two methods are useless, because in radiated cases cancerous involvement of the nodes is rarely confirmed by pathologic examination, and results on the treatment of "palpable nodes" mean nothing. As already pointed out, the presence or absence of palpable nodes is not to be depended upon as a reliable guide to the presence or absence of metastases. Tongue cancer rapidly metastasizes, and prognosis depends more than anything else upon the presence or absence of node involvement. Without node involvement, we should expect over 30 per cent five year "cures" in unselected cases; with node involvement the five year "cures" probably average well under 10 per cent. Successful treatment must depend upon keeping ahead of the disease, or, in other words, preventing extension of the disease to the neck. Thorough surgical removal of operable cervical nodes, whether palpable or not, seems a more rational procedure for accomplishing this than treating necks by external radiation, which is of questionable value except in the presence of very radiosensitive metastases, and then performing a neck dissection or using radium implants after metastases are thought to be present. For inoperable nodes, however, radiotherapy is of some value in prolonging life and occasionally producing a cure in the more radiosensitive forms.

The average duration from the onset of symptoms to the time the patient seeks relief with tongue cancer is still much too long to expect good results from treatment. This seeming neglect on the part of the patient is difficult to understand when it is considered that the mouth is one of the cavities of the body most accessible to inspection, and that cancers of the tongue are usually preceded by abnormal changes which are present for a considerable time before malignancy develops. Until the public is educated regarding the importance of mouth hygiene and the necessity of obtaining medical advice promptly when unusual conditions develop and persist about the mouth or tongue, the percentage of "cures" probably will continue to remain low.

The author gratefully acknowledges his indebtedness to Miss Mary F. Twining for abstracting articles from the literature on cancer of the tongue and for assistance in the preparation of the statistical data for this paper.

REFERENCES

[1] Quick, Douglas: Management of Cancer of the Mouth and Cervical Lymph Nodes. Am. J. Roentgenol. **31**, 366–377, March, 1934.

[2] Lane-Claypon, Janet E.: Reports on Public Health and Medical Subjects, No. 59. Ministry of Health, London, 1930.

[3] Frank, L. W., Enfield, C. D., and Miller, A. J.: Carcinoma of the Tongue in a New Born Child. Am. J. Cancer, **26,** 775–777, April, 1936.

[4] Belote, C. H.: The Association of Carcinoma of the Tongue and Syphilis. J. A. M. A., **94,** 1985–1986, June, 1930.

[5] Fraser, John: Carcinoma of the Mouth and Tongue. ANNALS OF SURGERY, **96,** 488–514, October, 1932.

[6] Fournier, J. A.: Sur la curabilitié du cancer en général et du cancer de la langue en particulier. Bull. de l'ac. de méd., Paris, **56,** 464–478, November 27, 1906.

[7] Lund, C. C.: Syphilis in Relation to Cancer of the Buccal Mucosa. New England J. Med., **209,** 131–134, July 20, 1933.

[8] MacGregor, J. A.: Malignancy of the Tongue on a Luetic Base. N. Y. State J. Med., **30,** 907–909, July, 1930.

[9] Meland, O. N.: Intra-Oral Cancer and Its Treatment. Radiology, **24,** 276–280, March, 1935.

[10] Raven, R. W.: A Study of Cancer of the Buccal Cavity with the End Results of Treatment. St. Barth. Hosp. Rep., **66,** 65–124, 1933.

[11] Simmons, C. C.: Treatment of Oral Cancer. Am. J. Roentgenol., **26,** 5–11, July, 1931.

[12] Pfahler, G. E., and Vastine, J. H.: Irradiation Therapy in Cancer of the Mouth, Technic and Results. Radiology, **22,** 15–26, January, 1934.

[13] Berven, E. G. E.: Development of Technic and Results of Treatment of Tumors of the Oral and Nasal Cavities. Am. J. Roentgenol., **28,** 332–343, September, 1932.

[14] Judd, E. S., and Phillips, J. R.: The Curability of Carcinoma of the Tongue. Proc. Staff Meet., Mayo Clin., **9,** 9–11, January, 1934.

[15] Blair, V. P., Brown, J. B., and Womack, N. A.: Cancer in and about the Mouth. Internat. J. Orthodontia, **16,** 188–209, February, 1930.

[16] Phillips, R.: Histology of Buccal Carcinoma in Relation to Prognosis and Radiosensitivity. Lancet, **1,** 118–122, January 17, 1931.

[17] Simmons, C. C.: The Treatment of Oral Cancer. Am. J. Roentgenol., **26,** 5–11, July, 1931.

[18] Lund, C. C., and Holton, H. M.: Carcinoma of the Buccal Mucosa. New England J. Med., **208,** 775–780, April 13, 1933.

[19] Semken, G. H.: Nelson New Loose-Leaf Surgery, **2,** 867–880, 1932.

[20] Blair, V. P., and Brown, J. B.: Treatment of Cancerous or Potentially Cancerous Cervical Lymph Nodes. ANNALS OF SURGERY, **98,** 650–661, October, 1933.

[21] Fischel, E.: Surgical Treatment of Metastases to Cervical Lymph Nodes. Am. J. Roentgenol., **29,** 237–240, February, 1933.

[22] Butlin, H. J.: The Results of Operations for Carcinoma of the Tongue, with an Analysis of 197 Cases. Brit. M. J., **1,** 1–6, January 2, 1909.

[23] Hartmann, P.: Traitement du cancer de la langue. Paris méd., **79–80** 326–332, April 4, 1931.

[24] Fischel, E.: The Treatment of Carcinoma of the Tongue. J. Missouri M. A., **27,** 541–546, November, 1930.

[25] Moure, P., and Martin, R. H.: Résultats éloignés du traitement chirurgical du cancer de la langue. Bull. Soc. franç. de dermat. et syph., **39,** 412–416, March 10, 1932.

[26] Brown, J. B.: Cancer about the Mouth. South. Surg., **3,** 47–50, March, 1934.

[27] Gask, E. E.: A Contribution to the study of the Treatment of Epithelioma of the Tongue. Lancet, **1,** 223–227, February, 1930.

[28] New, G. B., and Figi, F. A.: Malignant Diseases of the Mouth, Pharynx, and Larynx. Surg., Gynec. & Obstet., **60,** 483–484, March, 1935.

[29] Patterson, N.: The Use of the Diathermy Knife in Malignant Diseases of the Mouth, Nose, and Pharynx. Lancet, **2,** 633–636, 694–698, September, 1934.

[30] Cade, S.: Radium Treatment of Cancer of the Tongue. Lancet, **2,** 630–632, September 20, 1930.

[31] Quick, Douglas: Radium and Surgery in Cancer of the Tongue. Brit. M. J., **2,** 944–947, December 6, 1930.

[32] Regaud, C.: Les épithéliomas de la cavité buccale; leur traitement par le radium et les rayons X. J. de méd. et chir. prat., **103,** 15–28, January 10, 1932.

[33] Berven, Elie: Résultats du traitement radiothérapique des cancers de la buccale cavité et du pharynx. Gaz. méd. de France (supp. Radiologique), 377–378, May 15, 1935.

[34] Roux-Berger, J. L.: Cancer de la langue (Statistique de la Foundation Curie). Bull. et mém. Soc. Nat. de chir., **58,** 1343–1345, November 19, 1932.

[35] Delrez, L., and Desaive, P.: Statistique des épithéliomas de la cavité buccale antérieure (langue plancher de la bouche, voûte palatine et face interne des joues). Liége méd., **27,** 721–736, June 3, 1934.

[36] Pfahler, G. E.: Treatment of Cancer of the Mouth by Surface and Interstitial Radiation. Radiology, **23,** 472–475, October, 1934.

[37] Fitzwilliams, D. C. L.: Modern Treatment of Carcinoma of the Tongue. West London Med. J., **35,** 195–210, September, 1930.

THE CARE AND CURE OF CANCER PATIENTS

BENJAMIN RICE SHORE, M.D.
NEW YORK

FROM SURGICAL DIVISION A, ST. LUKE'S HOSPITAL, NEW YORK CITY, N.Y.

IT IS difficult to understand why the term palliation, or palliative treatment, has been applied in a rather derogatory sense to the care of cancer patients for whom a lasting cure is thought impossible. Few clinicians would be so bold as to talk about the cure of patients with valvular heart disease, arteriosclerosis, diabetes, or nephritis, even though by energetic and thoughtful medicinal therapy and by careful regulation of patients' lives many useful and happy years may be given to these unfortunate individuals. So far as I know, the expression "palliative treatment of cardiac disease" or "palliative treatment of diabetes" does not exist, and rightfully so, when in fact, the chance of a cure in these conditions is less than in many types of cancer. All individuals eventually die, and the result of the treatment of any disease can only mean postponement of this event. In spite of this, elimination of death—or something that is inevitable—is the sole criterion by which the care of cancer patients is often judged. What of the ones for whom life has been made more comfortable, mentally and physically, over a period of months or years by judicious surgery or radiation? Can their therapy not also be called successful even though they do not survive to be classed as three, five, or ten year "cures"?

In the fall of 1931 a young girl, with a melanoma in the skin above the right breast and a large mass of metastatic melanoma in the axillary lymph nodes, was referred to me for operation. The axillary tumor was growing rapidly and was causing pain and discomfort because of its size and position. The patient knew what she had and was desperate in her determination for operation. A painstaking and thorough dissection of the right axilla and wide excision of the primary tumor was performed even though at the time early recurrence seemed inevitable. It is not the fact that this patient was well and without signs of recurrent tumor three years later which I wish to record, but rather the fact, that had she survived only one or two years after operation, the mental and physical relief experienced by this girl was sufficient to classify this with the most satisfactory surgically treated cases of cancer. Had the patient died at the end of two years her case would never have been listed in the group of three or five year "cures" of melanomata, even though in many ways, considering the size and extent of the axillary metastases, her treatment was just as successful.

Recently one of my patients died of pulmonary metastases from cancer of the breast ten years after the original mastectomy performed by Dr. William A. Downes. The scar resulting from the operation remained well

---

Submitted for publication June 18, 1936.

healed until the rather injudicious use of radium in another clinic, for an obviously incurable metastasis in the sternum. This caused necrosis of the bone and overlying skin which must be considered rather the result of the treatment than of the disease. In spite of this, and in spite of the fact that the patient eventually died of her cancer, can anyone deny that the original treatment of her breast cancer was satisfactory?

The biology of the patient and of the individual tumor are two absolutely unknown and all important factors which are present in every case of malignant disease. It is true that certain structural and growth characteristics may give some indication as to the biology of a given class of tumors, although it must be remembered that little can be said with assurance about any one case. This is, of course, true of many diseases, especially the infectious ones, where individual immunity and resistance play such all important rôles. Prognosis in every instance must be guarded, as frequently the most desperately ill patients will recover. The point which I would like to emphasize is that in treating cancer patients we are treating, in each individual case, absolutely unknown qualities and quantities, and the best results can be obtained only by the unrelenting surgical, radiologic, and medicinal care of all patients.

Specific agents for the cure of human diseases are few in number and are applicable to a relatively small number of sick individuals. Various serums for some of the infectious diseases, quinine for malaria and salvarsan for syphilis, are about all. In some cases of primary anemia, liver seems almost specific, not in curing the disease but in relieving the symptoms, for when the liver is discontinued for any length of time the normal course of the disease is resumed. Death from diabetes has been postponed for many patients and in this prolonged period of time they may die of accident or other disease, but, in the main, such an agent as insulin has not decreased the death rate from the disease for which it is supposed to be specific. In other words, insulin in the treatment of diabetes does nothing more than surgery and radiation in cancer. The following comment by Joslin[1] is interesting in this connection: "Deaths from diabetes are said to be increasing, despite the discovery of insulin, but if you will analyze the statistics you will find that the mortality is increasing at the right end of life, namely, the older ages. Since insulin was discovered our Massachusetts statistics show that deaths from diabetes have diminished for all ages up to 50 years and the increase has been confined almost exclusively to individuals between 60 and 70 years of age or older. In other words, young diabetics are living, whereas the older diabetics have not acquired immortality." Therefore, in the light of the study of other diseases it would seem that an absolute and all inclusive specific agent for the cure or treatment of cancer patients is something which cannot be anticipated, but if such an agent should be discovered it will make a rather unique chapter in the history of the treatment of chronic diseases.

It seems reasonable to believe that the only true method of estimating the value of all forms of treatment of cancer is the study of the end-results secured in the treatment of all patients applying for admission to any given clinic or institution. Instead of that, reports of the results of very selected groups of cases are continuously being published. Would it not be instructive and highly interesting for our larger clinics for malignant disease to furnish us with the results of all patients treated, whether by radiation, surgery, or both, and regardless of whether the cases were considered favorable or not? This would eliminate entirely the personal element of the physician in the choice of suitable cases and would also eliminate the tremendous error which is recognized by all to exist in the clinical or pathologic grading of tumors. In other words, the end-results obtained in the treatment of all patients with cancer are far more important than the results obtained in a few, selected, favorable ones.

In 1928, I studied and reported the operability of 1,000 unselected patients with cancer who applied for admission to St. Luke's Hospital from July 1, 1923, to January 1, 1927.[2] Sixty-two of these were declined in the admitting office as too hopelessly advanced for admission, 299 were cared for on the medical and surgical wards as too advanced for operation, seven refused operation, 255 had operations for the relief of symptoms only, 87 had purely exploratory operations, and complete eradication of the tumor was

TABLE I

RESULTS SECURED IN THE TREATMENT OF 744 CONSECUTIVE CASES OF MALIGNANT DISEASE.

					Operable Cases					
Site	Total Cases	Operable Cases	Per Cent of Operability	Operative Deaths	Not Followed Over 2 Years	Followed	Known to Have Lived 3 Years	Known to Have Lived 5 Years	"Inoperable Cases" Lived 5 Years	Per Cent 5 Year Cures of All Cases
Breast	142	72	50.7	1	15	56	39	26	6	22.5
Stomach	109	18	16.5	9	6	3	1	0	0	0.0
Colon	52	21	24.7	12	1	8	6	4	0	7.6
Rectum	49	14	28.5	4	3	7	5	5	0	10.2
Uterus, cervix	73	12	16.4	0	5	7	4	2	0	2.7
Uterus, corpus	21	8	38.0	2	2	4	4	3	0	14.2
Skin	16	11	68.7	0	4	7	6	3	0	28.7
Lips	12	11	91.6	0	2	9	6	4	0	33.3
Ovaries	27	5	18.5	0	2	3	1	1	0	37.0
Gallbladder	9	2	22.2	1	0	1	1	1	0	11.1
Kidney	10	1	10.0	0	0	1	1	1	0	10.0
Tongue	3	2	66.6	1	0	1	1	1	0	33.3
Tonsil	3	1	33.3	0	1	0	0	0	0	0.0
Penis	2	2	100.0	1	0	1	1	1	0	50.0
Vulva	4	1	25.0	0	1	0	0	0	0	0.0
Fascia, sarcoma	6	1	16.6	0	0	1	1	0	0	0.0
All others	206	0	00.0	0	0	0	0	0	0	0.0
Totals	744	182	24.4	31	42	110	77	52	6	7.8

possible in only 320, or 32 per cent of the 1,000 patients. It is the follow-up of this same group of patients which I wish to report now. Unfortunately, 255 of the entire group were private patients and must be eliminated from our study because of the lack of accurate follow-up statistics. One other patient has also been eliminated because her tumor has since been judged benign, which leaves a total of 744 to be discussed (Table I).

In this unselected group of 744 consecutive patients with cancer admitted to the medical and surgical wards of St. Luke's Hospital, only 182 growths, or 24.4 per cent, were operable. Exploratory laparotomies, certain operations for the relief of symptoms, as colostomy, gastro-enterostomy, and gastrostomy, and the taking of biopsies were done in many of the so called inoperable cases, but in only 24.4 per cent of the entire group was an extirpation of the growth performed in the hope of a cure. This is distinctly lower than the operability in the group of 255 private patients who have been eliminated from this series. In this latter group, 137, or 53 per cent of the growths were operable. Several factors enter into this enormous difference in the two classes of patients. In the first place, the majority of private patients are seen by their surgeon before coming to the hospital and it is reasonable to suppose that many of the hopeless cases are eliminated in this way and spared the cost of hospitalization. This is no way true of ward patients, many of whom are admitted through the general admitting office for the sole purpose of consultation and hospitalization. There can be no doubt, however, that the majority of private patients do present themselves earlier for diagnosis and treatment, and in this way earlier and more operable cases are seen. If this is an important factor, one would expect an increase in the next few years in the inoperable cancer cases seen in private practice, the result of delay in consulting a physician due to the economic depression. It can only be suggested in conclusion that patients able to pay for private care in our larger city hospitals may also have been able and willing to pay for better and more expert medical advice, the result being earlier detection of cancer. In general, it must be said that an operability of only 24.4 per cent of such a series of ward patients is a deplorable condition and explains in the beginning the small percentage of five-year survivals obtained. Education, first of the medical profession, and second of the laity, is the only means of correcting such a condition.

Of the 182 patients operated upon with the idea of a cure, 31 died as the immediate result of the operation, an operative mortality of 16.9 per cent. This leaves only 151, or 20.2 per cent of the original 744 patients who were discharged from the hospital with any assurance of the possibility of outliving their disease for a period of years.

Follow-up of ward patients in such a city as New York with its ever changing and moving population is extremely unsatisfactory. Language difficulties, and the frequently suspicious attitude toward all investigators, make the tracing of patients who refuse or neglect to attend the regular follow-up clinics well nigh impossible. In this series we have been able to follow and repeatedly examine 110 of these 151 supposedly cured patients. Seventy-seven are known to have lived three years and 52 five years. To these must be added six patients with advanced and "inoperable" breast carcinomata who survived five years after what were considered at the time to be purely palliative mastectomies. This makes a total of 58 known five year survivals or 37 per cent of all the patients surviving radical operations, and 7.8 per cent of the entire group of 744 (Table I).

The actual number of five year survivals is obviously greater than the known 58. It is reasonable to suppose that approximately 37 per cent of the untraced 42 patients surviving radical operations lived five or more years, and it is possible and very probable that some of the patients with inoperable but radiosensitive tumors were treated by radiation elsewhere after their discharge from St. Luke's Hospital and remained well for five years. This is certainly true of some of the patients with advanced carcinomata of the cervix uteri who were referred directly to other well equipped clinics for radiotherapy. All of these patients upon whom no operation was performed have been lost to our follow-up clinic. Correcting our figures, then, to allow for the same percentage of cures in the 42 untraced patients as in the followed group, and to include a few conjectured but absolutely unknown cures from radiation in some of the inoperable cases, it would seem that ten per cent five year survivals of the 744 original cases would be nearer the real truth. This is indeed a small number and illustrates my original thesis that our problem at the present time is by necessity more the care than the cure of cancer patients.

For purpose of discussion I have divided the 58 five year survivals into the following six main groups: (1) five miscellaneous, totally unrelated cases; (2) seven carcinomata of the skin and lips; (3) five of the uterus and cervix; (4) nine of the gastro-intestinal tract; (5) 26 operable carcinomata of the breast; and (6) six inoperable carcinomata of the breast. In all of these the diagnosis has been made by histologic study of the specimens.

Several of the cases in the first group are self-explanatory and need no discussion. One patient with a carcinoma of the tongue, in whom local excision of the growth only was performed, is living and well eight years later. Another patient in whom an early carcinoma of the gallbladder was found unexpectedly on histologic examination of the specimen is well after eight years. Perhaps one of the most interesting cases of the entire series is that of a man, age 60, with a hypernephroma of the left kidney. The kidney removed by Dr. Frank Mathews measured 21x13x8 cm. and was almost entirely replaced by tumor. At the time of operation the prognosis for this patient was thought to be extremely bad, yet he has remained well for seven years. This case illustrates well the value of unremitting treatment of all cancer patients because of the impossibility of correct prognostication in every case (Table II).

Table II

GROUP 1. FIVE YEAR SURVIVALS—MISCELLANEOUS CASES

	Age	Location of Lesion	Results
(1). E. S.	48	Epithelioma of tongue	Local excision. Well 8 yrs.
(2). H. S.	62	Carcinoma of gallbladder	Cholecystectomy. (No gross tumor. Sections show early carcinoma.) Well 8 yrs.
(3). W. McS.	63	Hypernephroma of kidney	Left nephrectomy. (Kidney measured 21 x 13 x 8 cm. and was almost entirely replaced by tumor.) Well 7 yrs.
(4). H. M.	29	Papillary adenocarcinoma of ovaries	Bilateral salpingo-oophorectomy. Living with recurrences 8 yrs.
(5). J. McG.	54	Epithelioma of penis	Circumcision and bilateral dissection of groins. Died after 9 yrs. with local recurrence and cerebral metastases

Table III

GROUP 2. FIVE YEAR SURVIVALS—LIP AND SKIN CASES

	Age	Location of Lesion	Results
(6). M. F.	41	Adenocarcinoma of labial nodes of upper lip	Local excision. Well 5 yrs.
(7). A. E.	51	Epithelioma of lower lip	Local excision. Dissection left side of neck. Living with recurrences in neck 5 yrs.
(8). T. B.	69	Epithelioma of lower lip	Local excision. Dissection on right side of neck. Well 7 yrs.
(9). R. M.	66	Epithelioma of lower lip	Removal of lip. Plastic repair. Died of distant metastases after 5 yrs.
(10). T. H.	61	Basal cell epithelioma of cheek	Local excision. Died with local recurrences after 6 yrs.
(11). E. C.	43	Basal cell epithelioma of forehead	Local excision. Well 7 yrs. after excision of recurrences
(12). J. S.	70	Basal cell epithelioma of preauricular region	Local excision with plastic repair. Well 9 yrs.

Table IV

GROUP 3. FIVE YEAR SURVIVALS—UTERUS AND CERVIX CASES

	Age	Location of Lesion	Results
(13). L. K.	53	Adenocarcinoma body of uterus	Panhysterectomy and bilateral salpingo-oophorectomy. Well 8 yrs.
(14). M. F.	66	Adenocarcinoma body of uterus	Panhysterectomy and bilateral salpingo-oophorectomy. Well 7 yrs.
(15). M. S.	45	Sarcoma of uterus	Supravaginal hysterectomy and bilateral salpingo-oophorectomy. Well 9 yrs.
(16). M. R.	37	Epithelioma of cervix	Excision of cervical stump. (Supravaginal hysterectomy 1 yr. previously.) Well 8 yrs.
(17). S. W.	34	Adenocarcinoma of cervix	Panhysterectomy and bilateral oophorectomy. Died with recurrences after 6 yrs.

The second group of seven carcinomata of the lips and skin (Table III) and the third of five carcinomata of the uterus and cervix (Table IV) are self-explanatory and require no further comment. The fourth group of nine gastro-intestinal cases is interesting mainly because of the localization of the growths. It is immediately seen that there are no five year survivals of 109 total cases and 18 operable ones of carcinoma of the stomach. One of these patients lived with recurrences for three years after operation. It is interesting to note that no patient in this series of colon and rectal cancers who has lived for five years after radical excision of the growth has subsequently died of recurrences. The one patient who survived seven years after resection of the cecum for carcinoma has recently died of pneumonia and at autopsy careful search of all the thoracic and abdominal organs failed to reveal gross or microscopic cancer. So far as one can say, this patient was truly "cured" of his cancer (Table V).

TABLE V

GROUP 4. FIVE YEAR SURVIVALS—GASTRO-INTESTINAL CASES

	Age	Location of Lesion	Results
(18). T. V. Z...	67	Gelatinous carcinoma of rectum	Resection. Well 8 yrs.
(19). C. C......	36	Adenocarcinoma of rectum	Resection. Well 8 yrs.
(20). S. McD...	49	Adenocarcinoma of rectum	Resection. Well 7 yrs.
(21). K. W.....	37	Adenocarcinoma of rectum	Resection. Well 7 yrs.
(22). F. J......	51	Adenocarcinoma of rectum	Resection. Well 5 yrs.
(23). G. P......	50	Adenocarcinoma of splenic flexure	Resection. Well 10 yrs.
(24). C. V......	59	Adenocarcinoma of sigmoid	Resection. Well 7 yrs.
(25). H. R.....	74	Adenocarcinoma of sigmoid	Resection. Died of pneumonia after 7 yrs.
(26). J. W......	54	Adenocarcinoma of cecum	Resection. Died of pneumonia after 7 yrs. No evidence of cancer found at autopsy

Few conclusions can be drawn from a study of the 26 operable breast carcinomata. The patients range in age from 26 to 75, the average being 48 years. The axillary lymph nodes were involved in ten, or 38 per cent of these cases, and no record of axillary lymph node examination was made in one (Table VI). However, the group of six so called "inoperable" patients with breast cancers who lived for five years, following what was thought at the time to be a palliative mastectomy, is extremely interesting and instructive. In all of the cases, large, advanced and often ulcerated growths were present and mastectomy was performed to rid the patient of a malodorous and painful breast. Notes to the effect that the cases were surgically "inoperable" so far as eradication of the disease was concerned appear on the operative records of five of the patients, while in one the growth was considered inoperable by me when I studied the history because the axillary fat and fascia were extensively involved with tumor. The axillary lymph nodes were involved in all. In no case was even the possibility of a

Table VI

GROUP 5. FIVE YEAR SURVIVALS—OPERABLE BREAST CASES

	Age	Type	Axillary Nodes Involved	Results
(27). G. C......	36	Scirrhous	Yes	Well 9 yrs.
(28). J. B......	67	Scirrhous	Yes	Well 8 yrs.
(29). S. M.....	45	Scirrhous	Yes	Well 8 yrs.
(30). S. B......	61	Mixed	Yes	Well 8 yrs.
(31). C. C......	63	Medullary	No	Well 8 yrs.
(32). M. H.....	42	Medullary	No	Well 9 yrs.
(33). E. B......	39	Medullary	Yes	Well 7 yrs.
(34). M. A.....	49	Medullary	Yes	Well 7 yrs.
(35). M. B.....	49	Medullary	No	Well 8 yrs.
(36). E. A......	47	Medullary	No	Well 7 yrs.
(37). M. H.....	58	Medullary	No	Well 10 yrs.
(38). P. W.....	56	Papillary	No	Well 9 yrs.
(39). T. N.....	56	Adenocarcinoma	No	Well 8 yrs.
(40). M. W.....	26	Adenocarcinoma	No	Well 9 yrs.
(41). L. G......	40	"Carcinoma"	No	Well 6 yrs.
(42). E. B......	68	Gelatinous	No	Well 10 yrs.
(43). E. S......	62	Adenocarcinoma	No	Well 9 yrs.
(44). M. M.....	47	"Carcinoma"	No	Well 9 yrs.
(45). J. S......	39	"Carcinoma"	Yes	Living with recurrences 9 yrs.
(46). H. B.....	48	Scirrhous	Yes	Living with metastases 7 yrs.
(47). H. H.....	42	Duct carcinoma	Yes	Opposite breast removed for carcinoma 4 yrs. later. Living with recurrences 6 yrs.
(48). F. F......	48	Scirrhous	?	Died after 7 yrs.
(49). E. C......	52	Medullary	No	Died after 7 yrs.
(50). C. R......	44	Scirrhous	Yes	Died after 6 yrs.
(51). C. A......	43	Scirrhous	No	Died after 6 yrs.
(52). H. C.....	75	Carcinomatous cyst	No	Died after 6 yrs.

five year survival entertained. Postoperative radiation was given in four cases. Three of this group of six patients are living without recurrences after eight years, one died of her disease after six years, another after seven years, and one died of heart disease seven years after operation (Table VII). These six five year survivals of such seemingly hopeless cases should make any surgeon hesitate before refusing radical surgery to patients with advanced breast cancer.

Finally, mention must be made of a small group of patients with subsequently proved benign lesions upon whom radical operations were performed for supposedly malignant disease. In two instances radical surgery was indicated because of the extent of the local lesions but in one case it was unnecessary. These operations were not exploratory in character but were performed with mental assurance on the part of the surgeon that he was dealing with a malignant neoplasm. These mistakes were in one instance dependent on misinterpretation of a biopsy specimen and roentgenograms, but in the other two cases they were due to lack of use of all available means

TABLE VII

GROUP 6. FIVE YEAR SURVIVALS—"INOPERABLE" BREAST CASES

	Age	Type	Axillary Nodes Involved	Results
(53). M. McM..	60	Adenocarcinoma	Yes	"Inoperable," almost ulcerating mass in axillary tail. Well 8 yrs.
(54). L. S......	48	Scirrhous	Yes	"Inoperable" large ulcerating growth. Well 8 yrs.
(55). M. McF...	22	Medullary	Yes	"Inoperable" large growth. Well 8 yrs.
(56). A. G......	42	Adenocarcinoma	Yes	"Inoperable" large ulcerating growth. Died after 7 yrs.
(57) B. O......	55	Medullary	Yes	"Inoperable" mass size of orange. Died of heart disease after 7 yrs.
(58). E. H......	39	Medullary	Yes	Axillary fat and fascia involved. Died after 6 yrs.

for correct diagnosis. There can be little surgical excuse, either practically or theoretically, for proceding with radical surgery for supposedly malignant disease without histologic diagnosis of a biopsy specimen. These specimens must be taken by the surgeon with care and thought, so as to give the pathologist suitable material upon which to base his opinion. He has no choice except to examine the material sent him and it is not his responsibility if some tumor tissue is not included in the specimen. I cannot decide whether it is a compliment or an insult to a pathologist to present him with a few cells or a fragment of tissue removed from a growth, or its neighborhood, and expect him to make a diagnosis of the lesion actually present in the patient. It seems very much like showing a clinician a fragment of a temperature chart and compelling him to guess at the remainder. Biopsy specimens of adequate size and from representative portions of a growth are surely best obtained by gentle surgical means, and, so far as I know, no experimental or surgical evidence has yet been advanced to show that this method is detrimental to a patient with malignant disease.

SUMMARY.—In this discussion I have tried to emphasize the fact that cancer is only one of several chronic noninfectious diseases and that its treatment differs in no essential way from that of the others. Prolongation of life with the maximum mental and physical comfort, rather than the elimination of death, is the supreme goal and can be obtained in the greatest number of cases only by the continued, painstaking, and thoughtful care of all patients. No patient is ever too ill, or his tumor too advanced, for some form of physical or psychic therapy, and no physician at the present time is in a position to forecast correctly the duration of life in all cases. The biology of the tumor and the biology of the patient are two absolutely unknown qualities and quantities, present in all cancer cases.

Fifty-eight five year survivals of 744 unselected, consecutive patients with cancer applying for admission to St. Luke's Hospital from July 1, 1923, to

January 1, 1927, are reported. This is only 7.8 per cent of the total number, but 37 per cent of the patients surviving radical operations. A review of these cases cannot help but impress one with the fact that a definite prognosis must be given with extreme care in every case of cancer, and that not infrequently a patient with an advanced and seemingly hopeless tumor will outlive his disease for a period of years.

I wish to express my thanks to the members of the Surgical Staff of St. Luke's Hospital for permission to study and analyze their cases.

REFERENCES

[1] Joslin, E. P.: Diabetes. Its Control by the Individual and the State. Harvard University Press, 1931.

[2] Shore, B. R.: Operability in Cancer. Statistical Study of 1,000 Cases. J.A.M.A., **90**, 1690–1692, 1928.

SUBASTRAGALAR ARTHRODESIS IN PARALYTIC DEFORMITIES

W. Russell MacAusland, M.D.

Boston, Mass.

FROM THE MAC AUSLAND ORTHOPEDIC CLINIC, BOSTON, MASS.

In the *Archives of Surgery* for February, 1929, the writer described a method of subastragalar arthrodesis for stabilizing the paralytic foot, and presented a preliminary report on seven cases. The operation, as that paper brought out, has the great advantage of providing for backward displacement of the foot, thereby establishing the better leverage for weight bearing that is often necessary to the paralytic foot. Now, after 11 years' experience with the method, it has been proved to the writer's satisfaction that in certain types of paralytic feet, this stabilizing procedure affords uniformly excellent results.

The purpose of this second report is to call attention again to this operative method, placing special emphasis upon the selection of the case and presenting a study of a series of 21 cases, included in which is the subsequent course of four of the cases previously reported.

Indications for the Operation.—The indications for this operation are definitely defined. It is applicable to paralytic feet in which the anterior muscle group has sufficient control to prevent drop foot, and in which either the posterior muscle group, or the peroneal muscle group that may be substituted for the gastrocnemius, is sufficiently strong to prevent calcaneus deformity. The posterior muscle group, to be efficient, need not have its full strength, for less leverage is required when the foot has been displaced backward at operation. When the peroneal muscle group is transplanted to allow its action to replace that of the paralyzed posterior muscle group, the substituted power makes it possible to plantar-flex the foot even to the extent of rising on the toes.

This method of arthrodesis is most successfully carried out in paralytic feet in cavus, valgus, or varus deformity associated with calcaneus. Strong peronei must, of course, be present to replace the heel cord. In the cavus foot the malposition is corrected at the time of stabilization by removing a plantar wedge from the calcaneocuboid region. Valgus or varus deformity is corrected by the removal of a section of bone from the subastragalar region, which varies in thickness on its inner or outer side depending upon the deformity to be corrected.

Another indication for this method is found in the extensively paralyzed foot that calls for stabilization.

Paralytic foot deformities in both the child and adult may be treated by this method. Primarily, of course, it is used in younger patients, the ages between 10 and 16 being the best period. Never should arthrodesis be attempted

---

Submitted for publication May 11, 1936.

before eight or ten years, since the formation of a bony ankylosis cannot be insured at an earlier age.

Operative Technic.—Before the arthrodesis is carried out, deformities should be corrected as much as possible by manipulative or minor operative measures.

The incision is made on the outside of the foot, beginning over the dorsal surface in the midtarsal region, curving below the external malleolus, and terminating over the Achilles tendon. Care is taken to cut below the astragalocalcanean joint in order to avoid severing the external lateral ligaments between the astragalus and the fibula. The skin and fascia on each side are dissected back.

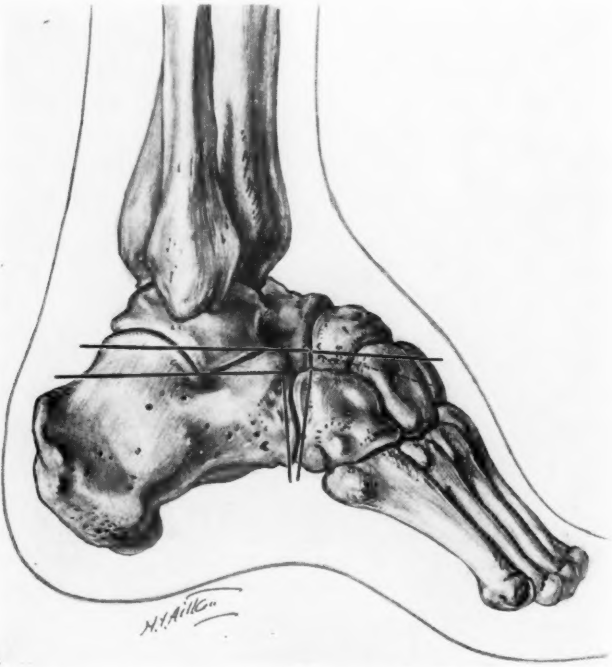

FIG. 1.—Diagrammatic drawing showing sections of bone removed from the os calcis, astragalus, and midtarsal and calcaneocuboid regions in the stabilization and correction of a foot in cavus deformity. Note.—The drawing is diagrammatic. The direction of the saw lines and the removal of the calcaneocuboid wedge will depend upon the deformity present. As little bone as possible should be removed.

The dorsal extensor tendons are retracted to the dorsum of the foot. The peroneal tendons are severed near their attachment and retracted; long sutures are inserted in their ends. The ligaments between the astragalus and the os calcis are severed. The capsule over the astragaloscaphoid joint and over the astragalocalcanean joint is opened. The sole of the foot is brought into marked inversion.

If cavus is present, a V shaped wedge with its apex directed toward the

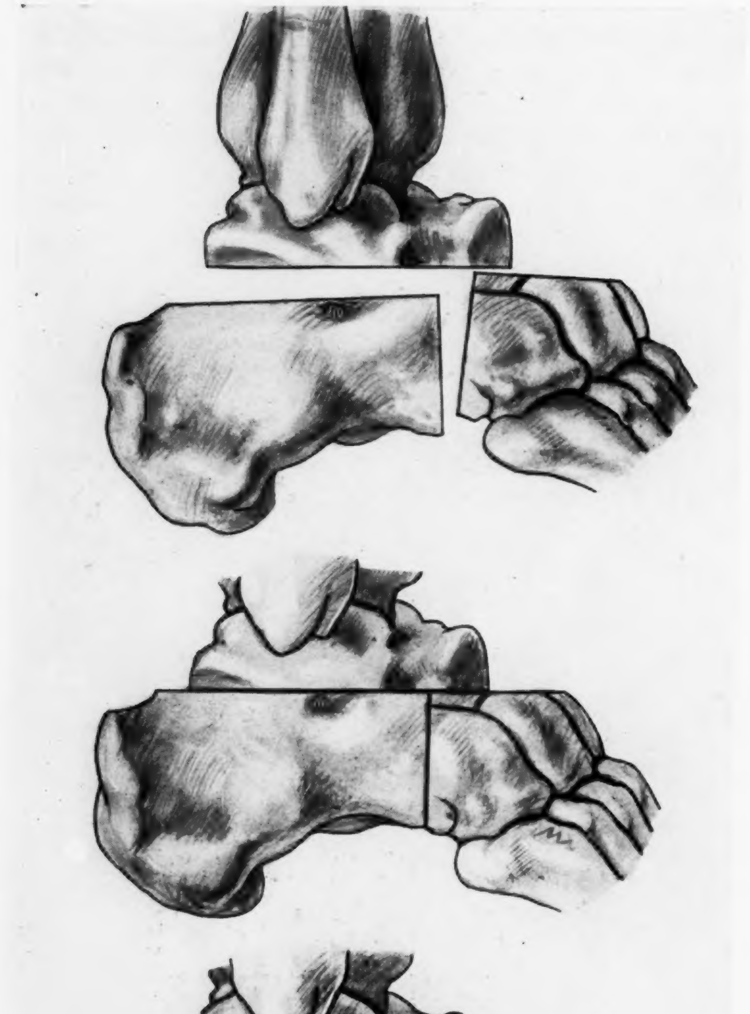

FIG. 2.—Diagrammatic drawings showing sections of bone removed and displacement of the foot backward. Note the dotted line indicating the removal of the protruding upper surface of the astragalus.

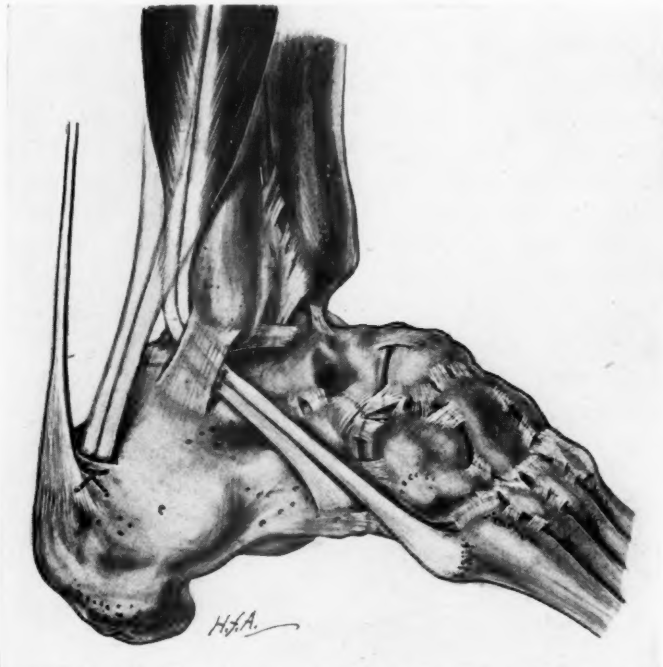

FIG. 3.—Transplantation of the peroneal tendons into the os calcis to replace the lost action of the Achilles tendon.

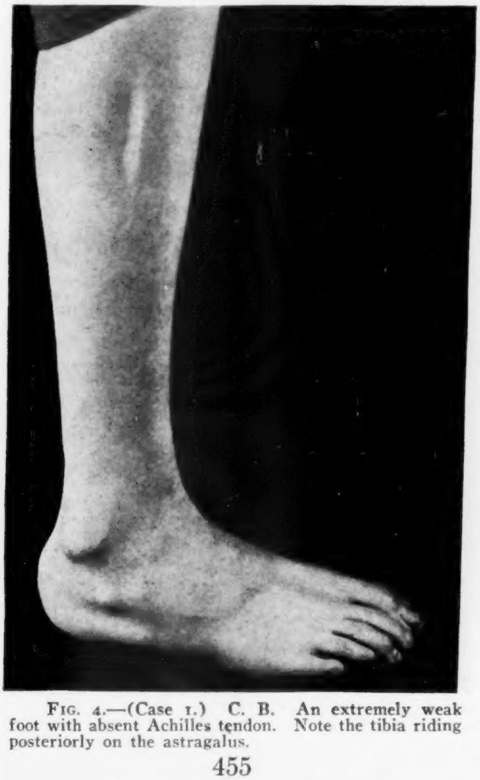

FIG. 4.—(Case 1.) C. B. An extremely weak foot with absent Achilles tendon. Note the tibia riding posteriorly on the astragalus.

plantar surface, and in size just sufficient to allow correction of the deformity, is removed from the calcaneocuboid region.

The entire body of the astragalus is brought into the wound after the ligaments on the inner side of the talus have been dissected upward. Care must be taken in so doing not to disturb the ligamentous attachments of the tibia, fibula, and astragalus. A small section of bone, larger on the inner or outer side depending upon whether the foot is valgus or varus deformity, is removed from the lower surface of the astragalus. A similar transverse section is removed from the upper surface of the os calcis.

The os calcis is brought temporarily into relation with the astragalus and the cavus wedge is closed. A section of bone is then removed from the scaphoid and upper tarsus, the saw line being made continuous with the plane of the flattened surface of the os calcis.

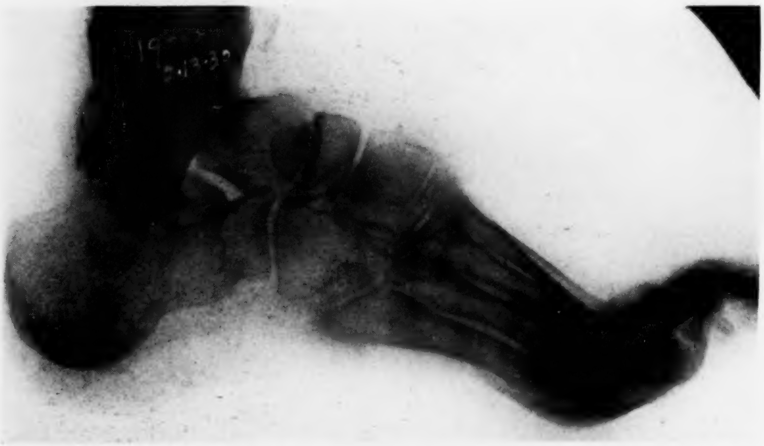

FIG. 5.—(Case 1.) C. B. Preoperative roentgenogram showing calcaneocavus deformity and tibia riding posteriorly on the astragalus.

The foot is displaced backward, and in so doing the remaining section of the scaphoid is brought in position to become arthrodesed to the overlapping neck of the astragalus. Any remaining prominence on the anterior superior part of the astragalus is shaved off (Figs. 1 and 2).

Where no cavus deformity exists, the operation is carried out in the same manner as described, except that no wedge is removed from the calcaneocuboid region.

If transplantation of the peronei is necessary, the tendons are fixed into the os calcis at the site of the attachment of the Achilles tendon (Fig. 3). The wound is closed in the usual manner.

A plaster of paris dressing extending from the toes to above the knee is applied, with the foot in five to eight degrees of plantar flexion. This position helps to maintain the posterior displacement of the foot. While the plaster casing is being applied the displacement backward is preserved by pressing

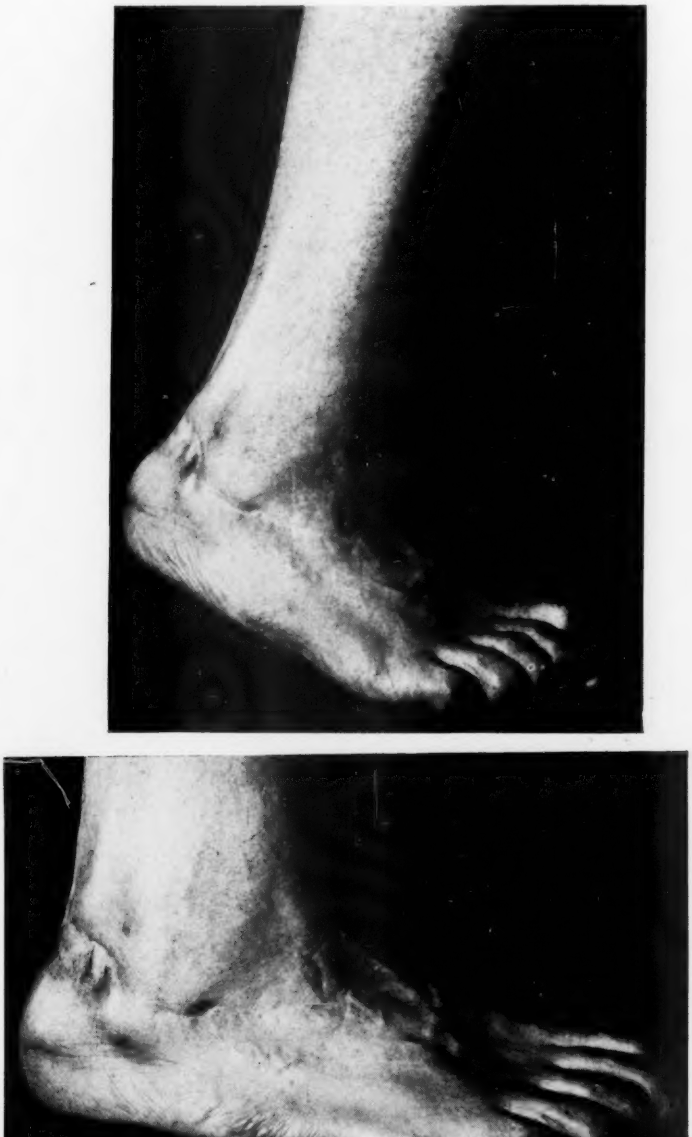

Fig. 6.—(Case 1.) C. B. Postoperative photographs taken six years after subastragalar arthrodesis. (A) Shows weight bearing with sufficient power in the transplanted peronei to support the full weight of the body in walking. (B) Shows the foot at rest.

with fingers on the sole of the foot and with the thumb on the bottom of the os calcis. The development of cavus is prevented by keeping the bottom of the plaster casing flat, while it is drying, with splint wood.

The foot is kept elevated, with the knee bent at the angle of 45 degrees, for ten days to three weeks. The plaster casing is then removed, the leg is brought into extension, and a new plaster bandage is applied from the toes to below the knee, with the foot at the right angle to the leg and in the position of slight valgus. Weight bearing is usually possible after six weeks. After ten weeks the plaster bandages may be discarded.

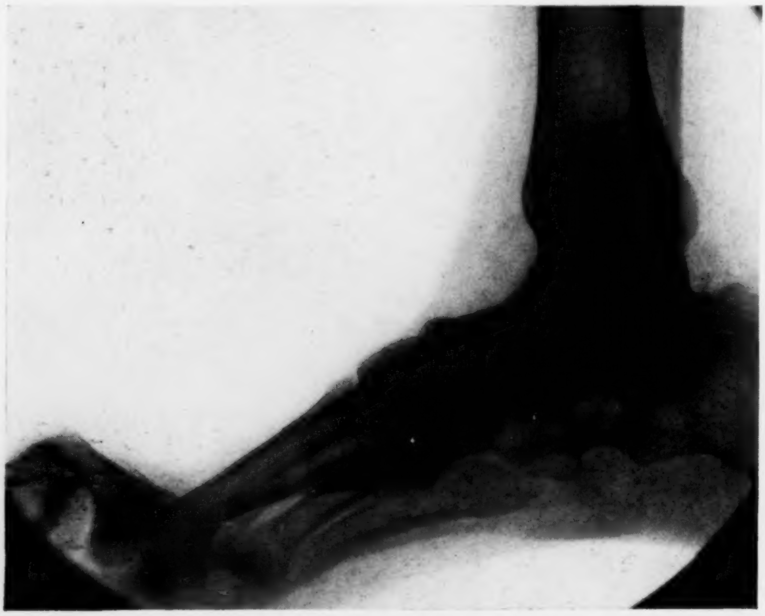

FIG. 7.—(Case 1.) C. B. Postoperative roentgenogram taken six years after subastragalar arthrodesis, showing the foot in corrected position, solid arthrodesis, and backward displacement of the foot.

The foot is then protected by a shoe equipped with an outer upright and a stop joint which holds the corrected position and limits motion. Physiotherapy, gradual use, and exercise are begun.

The total number of arthrodeses of this nature that have been performed at our clinic is 21. End-results are available on 16 of these cases.

In this group of 16 cases there were 11 children who, at the time of operation, were between the ages of ten and 18 years. In one case of a child ten years of age, the operation was carried out on both feet for the correction of valgus deformity. The other four patients were in their early twenties.

In five cases calcaneocavus deformity predominated; in six cases the foot was in calcaneovalgus; in three cases, including the bilateral case, the foot was in valgus; and two patients had generally weak, unstable feet.

Final examination of the 16 cases was made after a period varying from eight months to 11½ years from the time of operation. In five cases more than 11 years had elapsed; in seven cases over five years had elapsed; in one case four years had passed; in two cases, one and two years respectively; and in one case, eight months.

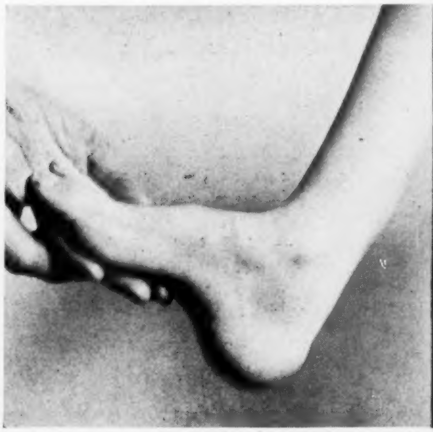

Fig. 8.—(Case 2.) T. L. Calcaneocavus deformity before operation.

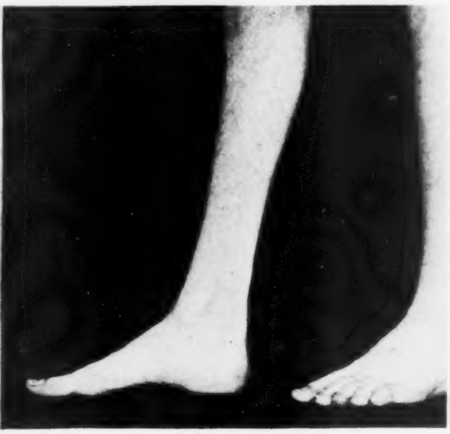

Fig. 9.—(Case 2.) T. L. Postoperative view taken 11 years after subastragalar arthrodesis, showing foot in corrected position. Patient has an excellent weight bearing foot and walks well without a limp.

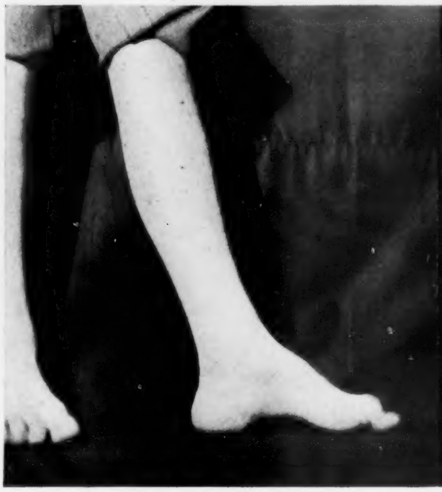

Fig. 10.—(Case 3.) S. P. Calcaneocavus deformity before operation.

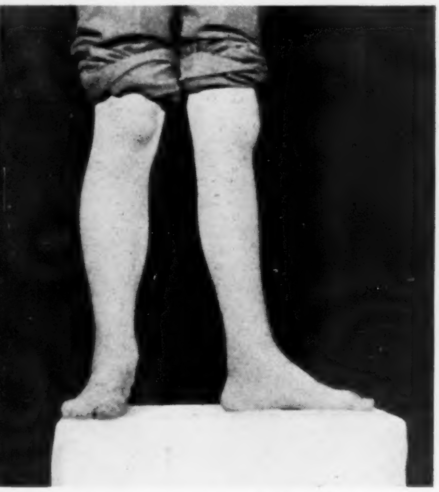

Fig. 11.—(Case 3.) S. P. Postoperative view taken six months after subastragalar arthrodesis, showing foot in corrected position. The patient has a stable, functional foot.

In the classification of the end-results, the term "good" is used to signify a case that has good stability, that has no symptoms and no limp, and the patient is able to walk without a brace. A study of the results based upon this criterion showed that all but one patient secured a stable, functional foot

Figs. 4 to 11). In the exceptional case the patient walks with the foot in varus deformity and is handicapped by the contraction of the great toe. This was one of the early cases of arthrodesis, and the failure to obtain an excellent outcome was due undoubtedly to imperfect operative technic.

CONCLUSIONS

By the use of the stabilizing method for paralytic feet herewith presented, both a functional, stable foot and the correction of deformity are insured.

Mechanically, the operation has the advantage of providing for backward displacement of the foot, a measure that is often necessary in paralytic feet in order to shift the line of weight bearing nearer the center of the foot. The procedure in no way interferes with the integrity of the ankle joint, nor is it followed by sensitiveness or arthritic changes.

The indications for the use of this operation are definitely defined. It is limited to cases in which the anterior muscle group has sufficient power to prevent drop foot, and in which the posterior muscle group, or the peroneal group that may be substituted, is strong enough to prevent calcaneus deformity. The operation may also be considered purely for stabilization of generally weak feet.

Twenty-one cases have been stabilized by this method. The end-results in 16 of these cases, which it has been possible to trace, have been uniformly favorable.

BRIEF COMMUNICATIONS AND CASE REPORTS

RETROGRADE JEJUNOGASTRIC INTUSSUSCEPTION THROUGH A GASTRO-ENTEROSTOMY STOMA*

EDWARD F. DUCEY, M.D., AND W. L. McNAMARA, M.D.
LOS ANGELES, CALIF.

FROM THE DEPARTMENT OF PATHOLOGY, VETERANS ADMINISTRATION FACILITY, LOS ANGELES, CALIF.

JEJUNAL intussusception through a gastro-enterostomy stoma is one of the rarer sequelae of the common operation for the relief of peptic ulcer, only 36 such instances having been reported in medical literature to date, including five in American publications.[1, 2, 3] Only four of the 36 were correctly diagnosed before operation, and in two of these the diagnosis was suggested to the physician by the patient, because of previous similar attacks with surgical intervention and cure. Of 37 cases (including ours), 28 were treated surgically, with 19 recoveries. Diagnosis in the nine unoperated patients was established at necropsy.

Bettman and Baldwin,[1] in 1933, were able to find 33 cases in an exhaustive review of the literature; two additional cases have been described by Adams,[2] and one by Chesterman.[3] Bettman and Baldwin, in their résumé, noted the following facts:

(a) The accident occurred as early as one year and as late as 16 years after the performance of the gastro-enterostomy.

(b) The size of the stoma bore no apparent relation to the incidence of the intussusception.

(c) The length of jejunal segment telescoped into the stomach varied from 5 to 200 cm., the average being 52 cm.

(d) The efferent loop was always involved; the afferent loop seldom.

(e) In only one case was the stomach examined fluoroscopically after ingestion of an opaque meal; in this instance the correct diagnosis was not made.

Case Report.—W. H., white, male, age 57, had had a gastro-enterostomy performed in 1920 for the relief of "ulcers," with complete symptomatic relief. He had no further complaints referable to the gastro-intestinal tract until September 5, 1935, when he was suddenly seized with epigastric colic of rapidly increasing severity, soon associated with retching emesis. The latter was clear at first, becoming blood tinged after about 18 hours; no clots or frank blood was noted.

On admission to the hospital, the patient was moribund and extremely dehydrated, with almost constant retching and hematemesis. Temperature 102° F., pulse 136, respiration 30. There was pronounced abdominal rigidity. No tumor masses were palpable. The blood count showed erythrocytes 6,080,000, leukocytes 18,000, with 83 per cent polymorphonuclears. The clinical picture suggested a perforated ulcer with peritonitis, the hematemesis being ascribed to trauma at the ulcer site from the pernicious vomiting. Sup-

---

* Published under R and P 6969. Submitted for publication May 9, 1936.

portive treatment failed to improve the patient's condition, and death ensued 30 hours after admission.

Necropsy revealed an early bronchopneumonia and moderate arteriosclerosis. The stomach was somewhat fixed by adhesions about the pyloric segment, and contained a sausage shaped tumor, which proved to be a loop of jejunum telescoped into the stomach through a posterior gastro-enterostomy opening, and which had undergone partial digestion. The loop involved the first 65 cm. of the efferent jejunal segment without implication of the afferent portion. The stoma measured 10.6 cm. in circumference. There was no evidence of active peptic ulcer, malignancy or peritonitis. A healed ulcer was found on the posterior wall of the duodenal cap. The vomited blood had come from eroded vessels of the digesting loop of intestine.

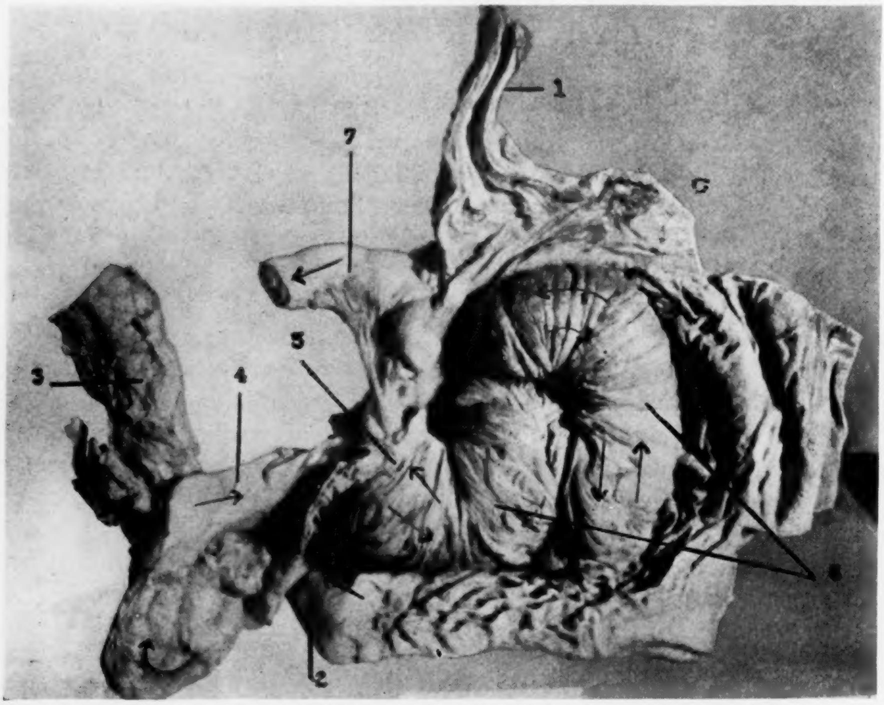

FIG. 1.—Dorsal view of specimen at necropsy. The posterior stomach wall has been cut away; the pancreas has been retracted lateral and twisted upon itself, to show the terminal duodenum entering the involved area. The directional arrows indicate the course of the intestine caudad from the pylorus. (1) Esophagus; (2) pylorus; (3) tail of pancreas, retracted lateral and upward; (4) third portion of duodenum; (5) site of stoma; (6) telescoped loop of jejunum filling stomach; (7) efferent jejunal loop.

COMMENT.—The above case is being reported, not only because of its interest as a pathologic curiosity, but also because the paucity of reported cases by American clinicians suggests the need of a greater familiarity with this condition on the part of both internist and surgeon. In Chesterman's case, a correct diagnosis of retrograde jejunogastric intussusception was made on the following criteria:

(1) The occurrence of acute epigastric colic in a gastro-enterostomized patient who had been symptom free from the date of his operation until the onset of the present illness.

(2) Repeated emesis of small amounts of blood intimately admixed with gastric secretions and with practically no clotted particles.

(3) Epigastric tumor without rigidity, fever, or leukocytosis, and with only local tenderness.

Chesterman stresses the diagnostic importance of this sequence of events, emphasizing the fact that colic is not a symptom of bleeding ulcer. In our case, the terminal condition of the patient on admission obscured the clinical picture, but the history was typically that outlined above.

SUMMARY

A case of retrograde jejunogastric intussusception is added to the series of 36 previously reported.

The syndrome of acute epigastric colic in an enterostomized patient, repeated hematemesis, and epigastric tumor without rigidity, is strongly suggestive of this condition.

Retrograde jejunogastric intussusception should be included in that group of unusual conditions to which the diagnostician frequently finds it necessary to refer during the study of a difficult case.

REFERENCES

[1] Bettman, R. B., and Baldwin, R. S.: J. A. M. A., **100**, 1228–1229.
[2] Adams, A. W.: Brit. M. J., **1**, 248, February, 1935.
[3] Chesterman, J. T.: Brit. J. Surg., **21**, 541.

SACRAL CHORDOMA*

ONE YEAR AFTER RADICAL EXCISION

BRADLEY L. COLEY, M.D.
NEW YORK

Case Report.—An American born female, age 63, first consulted me March 15, 1934, for pain and swelling in the right buttock. Her family history was irrelevant. Past History.—She had had a perineal repair 36 years ago; appendectomy 13 years ago; and a hemorrhoidectomy three years ago. The present illness dated from a fall down a flight of stairs six years before, when she struck the lower end of her spine. Following this accident she states it was painful for her to sit down or put any weight on this region. Two years later she again slipped and fell down the same staircase, injuring the same region. Three months before she first consulted me she noticed a swelling in the right buttock and adjacent sacral region, and during the few months prior to her visit to me she had constant pain in this region. Roentgenograms revealed a destructive lesion of the lower end of the sacrum and proximal segment of the coccyx, which presented a moth eaten appearance with no evidence of repair or bone production. The appearance was suggestive of a neoplasm. An aspiration biopsy was performed. Pathologic report by Dr. Fred Stewart of the Memorial Hospital: "Aspiration yielded many small cells incorporated in a mucinous base. In the midst of the small cells are rather pale vacuolated cells, which are consistent with a diagnosis of chordoma."

---

*Presented before the New York Surgical Society, April 22, 1936. Submitted for publication June 30, 1936.

Because of the unfavorable results following surgery in most of the reported cases of Chordoma, the patient was referred to Dr. Wm. G. Herrman, the radiologist, of Asbury Park, N. J., with the suggestion that irradiation therapy be attempted. During the following year Doctor Herrman treated the patient with high voltage roentgen ray given as follows: In late March and early April, 1934, she received a series of fractional treatments, using two portals anterior and one posterior; the two anterior directed at the tumor, and the posterior given directly over it, giving a total of 1,594 r units to each portal. In July, 1934, a smaller series was given, a total of 855 r units anteriorly and 824 posteriorly, using two portals, the anterior being directly opposite the posterior. One year later Doctor Herrman again referred the patient to me because of the steady increase in the size of the tumor and constant pain, which was not relieved by irradiation therapy.

Examination March 12, 1935, showed that there had been a tremendous increase in the size of the tumor since the previous examination. There was now a large, firm swelling extending from a point close to the tuberosity of the ischium across to the outer aspect of the posterior part of the buttock. It was only slightly movable. Rectal examination did not reveal any encroachment into the pelvis. The bulk of the tumor and the fact that it made sitting down almost impossible, together with the failure of irradiation to hold it in check or to relieve symptoms, prompted me to advise an attempt at surgical removal, particularly since recent stereoscopic films still showed the area of bone destruction confined to the fourth and fifth sacral segments and the coccyx.

She was admitted to the Ruptured and Crippled Hospital March 19, 1935, where laboratory studies showed normal blood sugar and blood urea. The red blood cells were 4,300,000; hemoglobin 74 per cent; white blood cells 5,850; polymorphonuclears 64 per cent; lymphocytes 36 per cent. Urine was negative except for a very faint trace of albumin. Blood pressure: 180/75. On March 21, 1935, under avertin anesthesia supplemented with nitrous oxide-oxygen, an incision was made extending from the left side of the sacrum across the midline to the right side and down the right gluteal region to the gluteal fold, a distance of some 25 cm. Through this incision the sacrum was exposed and divided through the fourth sacral segment with a chisel, the line of division being palpably proximal to the upper limit of involvement. The anterior surface of the sacrum was freed of areolar tissue overlying the rectum which was separated without damage. The dissection was then carried down along the gluteal region so that the entire tumor was eventually excised en masse and the wound closed. A small rubber dam drain was inserted which extended down to the dead space adjacent to the rectum which could not be completely obliterated when the skin over the sacral area was approximated.

Pathologic Examination.—March 21, 1935. The old sections showed a tumor composed of large islands of a substance resembling a typical hyaline cartilage. These islands are walled off by trabeculae of dense fibrous tissue. The cartilage is atypical in that many of the component cells are vacuolated and resemble the "signet ring" cells with an eccentric peripheral flattened nucleus. In the more recent sections the same picture is seen. Vacuolization of two or more cells is noted in certain areas, giving a pseudoglandular appearance. The histologic picture seems identical with that of the sacrococcygeal chordoma as described by Stewart, Ewing and others. *Diagnosis.*—Chordoma.

The wound healed satisfactorily without infection. The drains were shortened on the second postoperative day and removed on the fifth. Discharged on the twenty-second day.

The patient has returned for examination at frequent intervals and at no time has she complained of any of her previous symptoms. There was some irritability of the bladder, with urinary frequency, during her stay in the hospital, but this rapidly subsided. She has no difficulty in controlling her bladder and rectum. At each examination a slight bulging at the site of the removed lower sacral segment was noted when the patient coughed, but there has been no increase in the degree of this bulging, noticed either by the patient or by the examiner. She has been able to do her housework.

Roentgenograms taken following the operation showed a smooth stump of the sacrum at the site of the removal and no evidence of pathologic bone in the remainder of the sacrum or the base of the pelvis or lumbar spine. There are no complaints of sensory disturbances.

While remnants of the chorda dorsalis, a specific embryonal tissue about which the vertebral column develops, are regularly found in the intervertebral disks in infants, it has been shown that they commonly persist at the base of the skull and in the coccyx. Virchow first described the small tumors originating from this tissue as "ecchordosis spheno-occipitalis."

The sacrococcygeal chordoma varies considerably in its gross anatomy. Occasionally this tumor grows forward into the pelvis, where it causes interference with bladder and rectal function, and pain from erosion of bone and infiltration and pressure on nerves. When, as in the case reported, the tumors grow outward, very large masses may appear outside the sacrum. The growth is slow, Stewart placing the duration of sacral chordomata at six and one-half years. Of 15 cases which survived operation, 13 soon developed recurrence, and he found only two cases surviving operation three and five years respectively. Chordoma simulates closely two much more common tumors, *i.e.*, myxochondroma and colloid carcinoma of the intestinal canal. In a case of the latter type it may be extremely difficult to distinguish it from gelatinous carcinoma of the rectum. Local recurrence, however, is the rule and a fatal termination is usual.

Doctor Pool, in 1924, presented a case of sacrococcygeal chordoma before the New York Society. In his case a palliative operation was followed by roentgen therapy and use of radium emanation placed in the wound, with regression noted in the size of the tumor. The patient was shown two and one-half years after the operation. Dr. John F. Erdmann, in discussing this case, cited his experience based upon three cases.

Mabrey, in 1935, collected 150 cases. He credits Wood with first reporting in America, in 1913, a case of sacrococcygeal chordoma. He is unable to account for the delayed onset of these cases, for the greatest incidence occurs in the fifth and sixth decades, and states that it is twice as common in men as in women.

In the sacrococcygeal group, Mabrey's figures of 36 deaths with 16 autopsies and ten metastases, 62.5 per cent, would tend to refute the accepted belief that metastases seldom occur. He concludes that treatment in the sacrococcygeal cases is surgical, whenever possible. While surgical removal is so frequently unsuccessful, irradiation is also of little value as these tumors—as one would expect from their histologic nature—are radioresistant.

This case is shown to illustrate a manner in which total resection of the fourth and fifth sacral segments, together with removal of the bulky soft part extension en masse, was apparently undertaken without unfavorable sequelae. At present the patient presents no evidence of recurrence.

DISCUSSION.—DR. JOHN H. GARLOCK (New York) stated that Doctor Pool's case was alive and well three and one-half years ago, which was ten years after the palliative operation.

DR. BYRON STOOKEY (New York) reiterated Doctor Coley's statement that chordoma occurs at either end of the vertebral column, in the sphenoid or in the sacral region. Differential diagnosis when the tumor is in the sphenoidal region is seldom possible until after operation, at which the conditions are found to be rather hopeless since it is not possible to remove the tumor and only palliative procedures can be employed. In the sacral region, disastrous results may certainly occur in attempting to remove the tumor, and if to remove it means destroying the innervation of the bladder and rectum, it is better for the patient, especially if it be a woman, to bear with the tumor. Doctor Stookey complimented Doctor Coley on his very skillful removal of the tumor and the excellent end-result, and, in conclusion, stated that Doctor Eckel of Buffalo had compiled a series of basosphenoidal as well as sacral chordomata, from the literature, which was most interesting.

TRAUMATIC ARTERIOVENOUS FISTULA OF THE PALM*

WILLIAM DE W. ANDRUS, M.D.
NEW YORK

Case Report.—Mrs. B. LeD. (No. 112252), white, age 23, was admitted to the New York Hospital October 17, 1935, complaining of a painless swelling on the palmar aspect of the left hand. This swelling was noticed shortly after the emergency suture of a laceration produced by broken glass three and one-half years previously. The patient had been conscious throughout this period of a buzzing sensation in the region of the swelling. Aside from this peculiar sensation of vibration, the condition of the hand did not trouble her until about one year ago when she noted that the veins of her hand and lower left forearm were becoming swollen and more prominent. This was particularly marked after using the hands in daily household work. She had also noticed that the left hand was usually warmer and more moist than the right.

The patient presented herself for surgical treatment because of the noticeable enlargement, the subjective sensation of buzzing and vibration, and the fear that injury to the swelling might cause hemorrhage. Her past history was irrelevant.

Physical Examination was not remarkable other than for the findings relevant to the left upper extremity. Examination of the local lesion found a swelling in the region of the hypothenar eminence of the left hand, where a stellate scar was also visible. This swelling was easily compressible, and exhibited a thrill and bruit both synchronous with systole. The swelling covered an area approximating 5 x 3 cm. in size and was raised 1 cm. above the surface of the palm of the hand. About it there were numerous dilated veins, which extended halfway up the forearm. The ulnar artery could be compressed proximal to this swelling and its compression caused a diminution in the intensity of the bruit, but this was not entirely obliterated unless both the radial and the ulnar arteries were compressed simultaneously. Roentgenologic examination of the bones of the hand and forearm showed no appreciable variation from the normal, and those of the soft tissues showed the arteries and the veins of the left forearm to be unusually large.

---

* Presented before the New York Surgical Society, January 22, 1936. Submitted for publication April 13, 1936.

The heart borders were within normal limits. A2 was greater than P2. A soft systolic murmur was heard over the apex. The systolic blood pressure in the left arm, on repeated observations, was ten to 20 points higher than that in the right arm, though there was no significant change in pulse pressure. Blood pressure before operation: 122/76 right arm; 132/80 left arm. Oscillometric readings on upper extremity were as follows: Right upper arm 10, right forearm 9; left upper arm 4, left forearm 3. Skin temperature over the left hand and the ulnar half of the left forearm was consistently four to five degrees higher than the same area on the right side. Special examinations with regard to the heart showed that the cardiac shadow on the roentgenogram was not unusual, and was not an evidence of cardiac enlargement. The electrocardiographic readings were reported as essentially normal. Erythrocyte, leukocyte, and hemoglobin counts were within normal. Uranalysis was normal and the serologic tests for syphilis were negative.

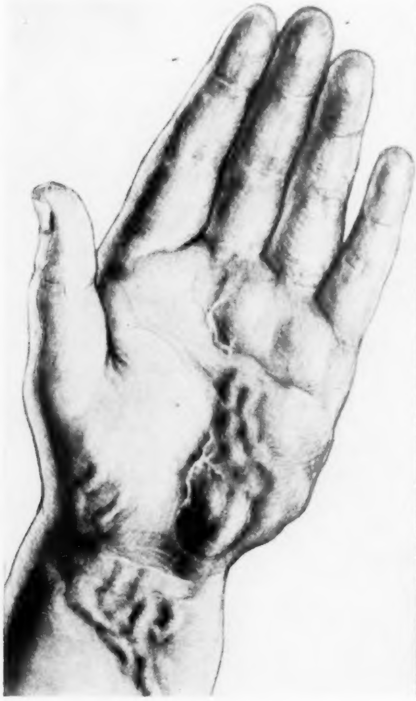

FIG. 1.—Drawing showing the dilated veins about the arteriovenous fistula.

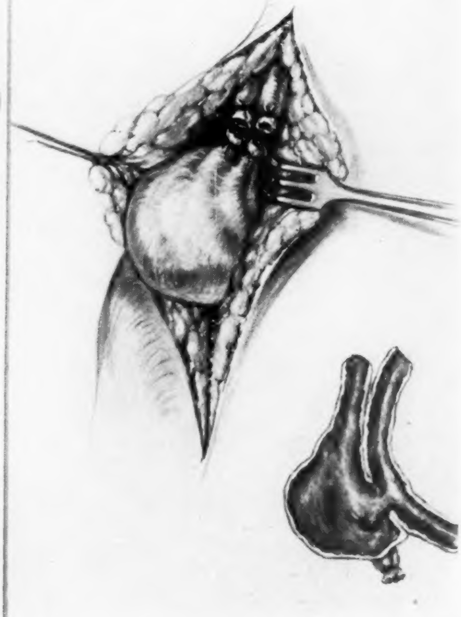

FIG. 2.—Drawing showing the exposure of the arteriovenous fistula, and the appearance on cross-section of the specimen.

Operation.—October 28, 1935. Under general anesthesia a tourniquet was applied to the left arm, and the palmar region explored through a curved linear incision 8 cm. long. Dissection revealed that the lesion was an arteriovenous fistula, between the superficial volar arch and the corresponding vein, with dilatation of the regional veins. Quadruple ligation of the involved vessels was performed with excision of the fistula bearing segments. A somewhat striking point in the examination of the fistula at operation was that the artery distal to the fistula did not vary appreciably in size from that proximal. It was the operator's impression that this was due to the large collateral circulation between the superficial and deep palmar arches. After the excision, the ligated stump of the ulnar artery could be seen to pulsate visibly and pulsation could be obtained in the radial artery.

Immediately postoperative, the patient stated that she was no longer conscious of the buzzing and vibrating sensation in the left hand. A transient tourniquet palsy occurred which cleared up before discharge from the hospital 16 days postoperative. Electrocardiograms taken after operation showed no striking variation from those taken preoperatively.

Pathologic Examination.—The specimen consisted of a small, rather thick walled vessel, 3.5 cm. long and 0.5 cm. in external diameter, threaded on a probe. At one end was a dilated aneurysmal mass resembling a varicose vein, measuring 2.7 cm. in length and 1 cm. in external diameter. On opening the sac it was found to be lined with smooth endothelium and to be composed of a large, dilated cavity with a beaded, tortuous, sac like extension several millimeters in diameter. The sac was quite empty and the point of communication with the larger vessel was extremely difficult to locate. It was finally found in the smaller sac like projection and measured slightly over 1 Mm. in diameter.

This patient illustrated very well the tremendous enlargement of the veins which may take place after the development of an abnormal arteriovenous communication, and the ease with which the condition may be rectified after elimination of the fistula. Fortunately the abnormal communication occurred between vessels around which there is very ample collateral circulation so that their ligation was attended by no untoward sequelae.

Dr. H. H. M. Lyle (New York) stressed the rarity of aneurysm of the hand in view of its rich circulation, the trauma to which it is frequently exposed, and the number of foreign bodies that have to be extracted from it. Since the presentation of a paper by him before the American Surgical Society, which was based on a study of 64 true aneurysms of the hand, the earliest of which dated back to 1837, two cases have been added by Doctor Matas, bringing the total to 66. In his search for cases with true aneurysm of the hand, he encountered a fair number of descriptions of a clinical variety of arteriovenous fistula that might be called a delayed type, that is, a congenital variety which seems to be activated by trauma, and which gives a very different prognosis and which is difficult to cure. Dr. J. Douglas presented such a case before the New York Surgical Society some years ago and the speaker had had one such case in addition to one he saw recently in consultation with Dr. W. MacFee. To emphasize the rôle of trauma, the following case was cited.

Case Report.—A boy, age 21, ran a fragment of glass into his hand, in 1920. In 1926 he broke his ring finger playing handball, and entered New York Hospital for treatment. The fracture was set and after three weeks the splint was removed, but the hand did not do well. The boy suffered a great deal of pain in his palm and there was considerable stiffness of all fingers. The condition was treated by heat and other usual measures, without improvement, until, 20 months later, he was admitted to St. Luke's Hospital, where a diagnosis of aneurysm of the palmar arch was made. He said that four weeks after the fracture he had consulted a dermatologist because the skin of the palm was becoming dark in color and the injured finger was turning blue. Six roentgen treatments had only aggravated the condition.

On admission, the skin of the palm and injured finger presented a typical picture of aneurysm. A very distinct bumblebee buzz was noticeable over the site of the old palmar scar. This sound was transmitted up the arm to the elbow and was accompanied by a typical thrill. The veins of the arm were dilated. On the assumption that the aneurysm was due to trauma, he explored the hand and found an arteriovenous aneurysm between the deep and superficial arches. This was dissected out and the surrounding vessels were tied off. The patient remained well for six months and then began to complain of pain in the hand, so severe that he could neither work nor sleep. The congestion of the veins in the fingers had increased and the bumblebee buzz had returned with increased intensity. Roentgenograms showed that the bony openings of the nutrient arteries in the third and fourth fingers were much larger than normal, and that there were progressive atrophy and absorption in the phalanges. A second operation was undertaken, in which the radial and ulnar arteries were ligated and severed and the superficial palmar arch excised. Again, there was an apparent cure, followed within ten months by return of the symptoms. In a third operation, the ulnar and radial arteries, as well as the communicating vessels, were excised down to the pisiform bone, on one side, and into the snuff box on the other. In short, in these three operations the ulnar and radial arteries, and the superficial and deep arches, were excised. The interosseous artery was intact and some of the vessels had split the ulnar nerve in two. The patient remained well for one year and the bumblebee buzz did not recur, but he began to have pain and swelling in his fingers. They became extremely painful and deep ulceration appeared on the third and fourth fingers. First, the fourth finger was amputated; then, later, the third. After this he was able to return to work and has remained well during the three and one-half years that have since elapsed, so that there is reason to hope that the cure is permanent.

Summarizing the case, Doctor Lyle said that over a period of five years he succeeded in blocking off some of the congenital arteriovenous openings, with temporary improvement, only to find, after a lapse of time, that other congenital openings had expanded, bringing about recurrence of the symptoms, which ceased only with the final operation described.

Dr. Wm. F. MacFee (New York) said that he had not had a case of traumatic aneurysm of the hand, but described a congenital arteriovenous aneurysm which he had treated, in which the communications were evidently multiple. The hand was operated upon a number of times. At each operation one or more definite aneurysmal dilatations were removed only to be succeeded by others developing at other sites. The index and middle fingers became spongy masses of dilated blood vessels and eventually had to be amputated. A considerable mass of palmar vessels near the bases of the fingers was excised at the time of the amputations. At present, the patient is free of symptoms and the circulation of the remaining portion of the hand appears to be relatively normal. There is no palpable or audible thrill and no pain. The sequence of events in this case followed the rule that amputations are necessary to effect relief.

PEDICLE BREAST FLAP FOR AMPUTATION STUMP

STRUCTIVE SURGERY APPLIED TO AMPUTATION STUMP AT KNEE

Johannes F. S. Esser, M.D.

Monaco

Case Report.—A. W., female, age 19, suffered an accidental amputation of her right leg, eight centimeters (three and one-half inches) below the knee joint. The wound would not heal, and no local skin or sliding flaps could be utilized, because of the probable formation of scar contractures. Furthermore, there was not enough of the proximal fragment of the tibia left to allow of a reamputation, without involving the knee joint itself.

Submitted for publication June 30, 1936.

Doctor Oidtmann of Amsterdam, under whose care she had been previously and who referred her to me for further structive procedure, had already, ineffectually, attempted to graft skin from the adjacent leg by placing the stump under a raised flap. Having had considerable experience in the use of a pedicle breast flap in successful plastic reconstruction of deformities during the past 15 years, I determined to employ this procedure in the present instance.

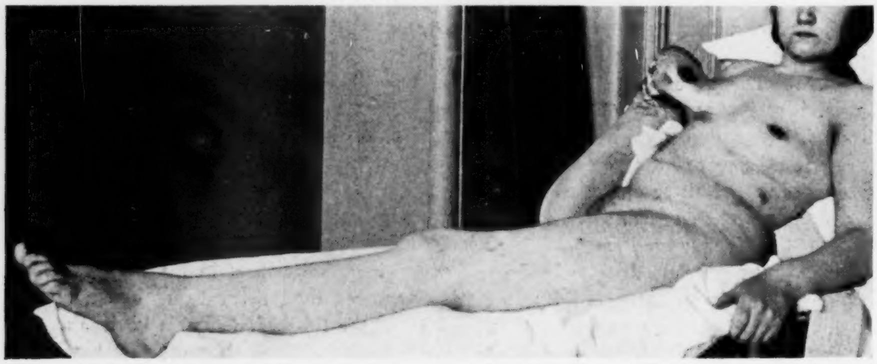

FIG. 1.—Showing posture necessitated in order to place the amputation stump of right knee in the incision in the right breast.

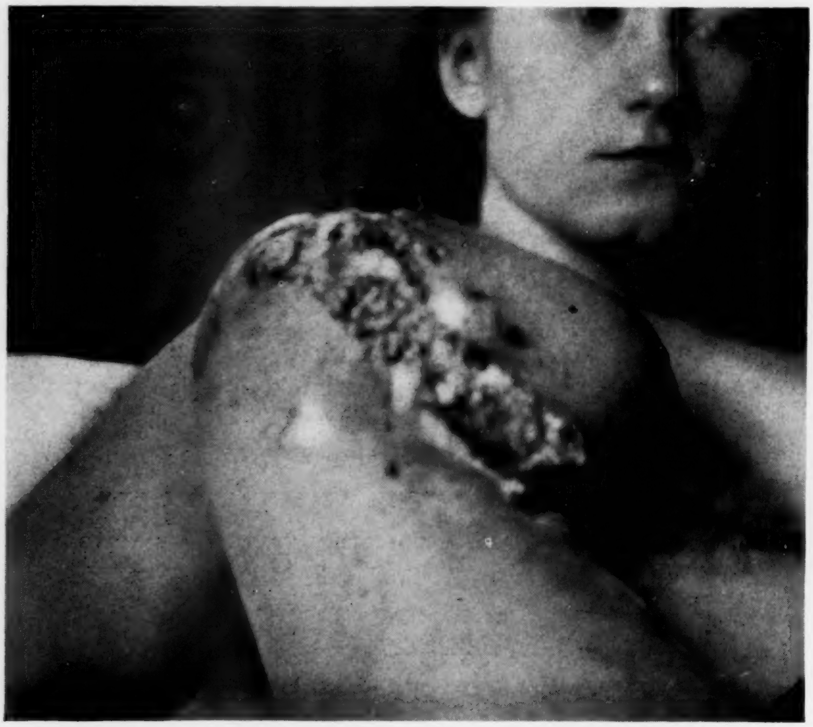

FIG. 2.—Showing, more in detail, the manner of the approximation of the knee to the breast incision.

The skin covering the female breast is much more ample than on any other part of the body, in fact, the reduction of it is considered a cosmetic advantage by many; and if one should wish the normal breast to be reduced in size, to conform to that of the partially amputated one, it can be readily accomplished. Indeed, it is seldom that, normally, both breasts are symmetrical. In the present instance, however, the patient did not object to the resultant postoperative deformity and refused to have it corrected and a plastic performed upon the normal one in order to make them equal in size.

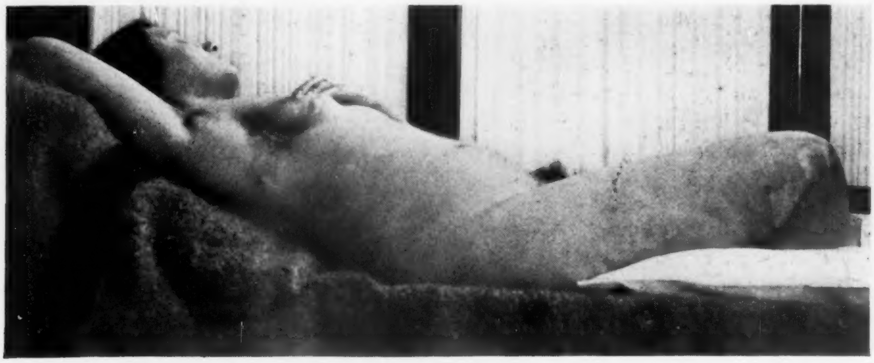

FIG. 3.—Showing the resultant scar in the breast and the well covered and healed amputation stump of the right knee.

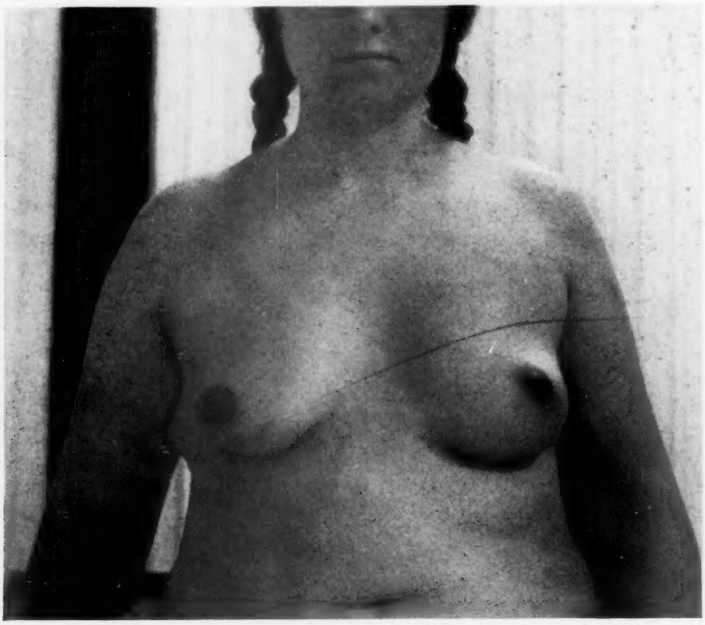

FIG. 4.—Photograph of the general appearance of the anterior view of the breasts.

In all cases where pedicled flaps have been utilized, after severance of the pedicle, some months must be allowed to elapse after the transplantation has been accomplished before the weight of the body should be allowed to press upon it; and the first exercises with the use of a prosthesis must be undertaken very gradually.

The transplanted flap is at first quite insensitive and its circulation is definitely impaired; therefore, in the beginning, the limb may only be exercised for very short periods at a time, and then only under rigid supervision. The primary requisite is to have an accurately fitted prosthesis which may only be obtained from a plaster mold of the healed stump.

The patient in question had, in the beginning, small ulcerations on the stump, the result of local pressure necrosis, because she used her leg too much and too soon. This may have been predisposed to because of abnormal perspiration of the affected leg.

A structive operation, as indicated in the illustrations, was performed in August, 1925. Ten years have now elapsed and the end-result is quite evident. She is quite content with her infirmity and is otherwise well.

PEDICLE GRAFT OF SOLE OF FOOT*

Wm. Crawford White, M.D.

New York

Case Report.—S. R., age 21, male, was injured 17 years ago in an automobile accident. He was admitted to the Lincoln Hospital suffering from multiple compound fractures of the toes with Cl. welchii infection. As a result, he lost his toes and considerable skin. The skin of the plantar surface posterior to the transverse arch became gangrenous and died. A skin graft operation was not permitted. It took six months for the raw areas to become covered over with thin epithelium on the plantar surface, with no soft tissue beneath. From then on, the patient had constant trouble with his foot. Ulcers formed and persisted for months, and infections were not infrequent.

Examination showed marked deformity of the right foot. The ankle joint was normal, as was the skin over the Achilles tendon. Hard skin was attached to the heel and sole of foot. He wore a shoe with a lining of rubber sponge and walked on the ball of his foot, with a slight limp. It was decided to apply a full thickness graft to the under surface of the foot, including the posterior surface of the os calcis. The delayed tubular graft was the method of choice.

At the Roosevelt Hospital, therefore, two parallel incisions eight inches long were made on the anterior surface of the left thigh. The subcutaneous tissue was freed from the underlying muscle sheath, after which the wounds were sutured. Fifteen days later, the oblong skin was folded under and the edges sutured to make a tube. This tubular graft was allowed to heal and nothing more was done for four months, because of a slight infection. At the end of that time, he had a tube about one inch in diameter and eight inches long. The skin was soft and pliable. At this operation, the distal end of the tube of skin was divided and the undersurface was split longitudinally and the edges everted. It measured two inches across. This was outlined against the sole of the foot. A corresponding area on the sole was then excised down to the plantar fascia. The right foot was now placed against the left thigh and the flap of skin sutured so as to cover over the raw area. The skin was covered with silver foil and rubber sponge pressure pads were applied over this. The limbs were held together by plaster bandage.

---

* Presented before the New York Surgical Society, March 25, 1936. Submitted for publication June 8, 1936.

Ten days later rubber covered stomach clamps were applied to the thigh end of the tubular graft to test the circulation. The clamp was left on for progressively longer periods. By the eighteenth day it was thought that the graft had taken and the skin was divided at its junction with the thigh. The tube was opened and the corresponding area over the heel was marked out and excised. The graft was then sutured over the raw area. There was some necrosis, but very little. A few days later the patient was allowed home on crutches.

It is now five months since the operation. Sensation has begun to return, although pain and temperature reactions have not yet reappeared. About two months ago I thoughtlessly gave the patient permission to walk, and due to lack of sensation he developed a pressure sore over the heel which took a long time to heal.

The condition is unusual, chiefly because of the trouble the patient had as there was no soft tissue under the skin, and illustrates the satisfactory results that may be obtained with the Gillies' delayed tubular, full thickness graft.

DISCUSSION.—DR. JEROME P. WEBSTER (New York) expressed the opinion that Doctor White had exercised very good judgment in not using free grafts, but a pedicle flap with a whole thickness of skin and fat, in order to give a pad to the bearing surface, particularly over the os calcis, and a delayed graft which increased the vascularization. A Gillies' tubular, pedicle flap is better in certain instances, even though it takes more time, because it avoids any possibility of infection. Frequently with a short tubed, pedicle flap, it is not possible to utilize as wide an area as when employing a simple, untubed flap. The difficulty with the latter is, of course, the added risk of infection. It is often possible to use a delayed, untubed pedicle flap which is retrograde, that is, the attachment is down toward the knee rather than up toward the hip. After delaying it in order to get a better vascular supply, it is brought further down so that the position is easier on the patient. As far back as 1497 Benedictus cautioned against the effect of the cold of winter on a new flap, and against pulling it off. The ulcer that occurred when Doctor White's patient put weight on the flap, before there was innervation to enable him to realize what pressure was doing to the flap, was a simple trophic ulcerative process.

DR. FENWICK BEEKMAN (New York) described a series of traumatic injuries, in Bellevue Hospital, in children whose feet had been crushed or the skin avulsed from the foot, and said that when, invariably, the loose phalanges had been removed and the foot left to granulate, the wounds would be pinch grafted after they had cleaned up, and would then heal. However, as the skin lay almost directly upon the bones, this procedure always proved to be unsatisfactory. Therefore, the method described by Doctor White has been used, that is, after the free grafts are put on, pedicle grafts are later applied to cover, more or less, the whole of the area, but especially those areas covering the bearing surfaces which are bound to break down. No attempt is ever made to place them on the granulation tissue for that would be too precarious. It is far preferable to wait until healing has taken place.

FRACTURE-DISLOCATION OF THE CLAVICLE*

Fenwick Beekman, M.D.
New York

The appended case report is presented to demonstrate the power of repair which occurs in children, following fractures, and also the ability to reproduce portions of bone which have been destroyed as the result of trauma.

Case Report.—W. E., age 11, a school boy, was injured October 9, 1935, by being crushed against a building by a truck, pinning his shoulder against the wall. He was admitted to Bellevue Hospital shortly after the accident, suffering from severe shock. On examination it was found that there was a lacerated wound over the left clavicle, which was actively bleeding. A clinical diagnosis was made of a compound comminuted fracture of the clavicle without protrusion of the bone through the wound. A large dressing was applied over the clavicle, which was bound tightly over the wound, and the boy was treated for shock.

Roentgenologic Examination demonstrated a fracture through the middle third of the left clavicle and a complete dislocation of the outer end of this bone. The distal fragment was composed of almost one-half of the clavicle and had been displaced so that it lay in a vertical position. There was also present a fracture of the glenoid fossa with the fracture lines running into the body of the scapula, with slight displacement of the fragments (Fig. 1).

A disagreement developed among the members of the staff as to what procedure would insure a satisfactory result. Forty-eight hours after the accident a tremendous hematoma had formed in the clavicular region and there was still some blood draining through the small wound over the clavicle. It was feared that the displaced fragment had lacerated the subclavian vein and, therefore, that a conservative course of treatment should be followed. Traction was applied to the left humerus by means of skin traction straps, to which a five pound weight was attached, and the arm abducted to 90°. It was felt by some of the staff that we should do something to correct the displacement of the fragment. Some wished to cut down upon it and excise it, others wanted to replace it and wire its distal end to the acromion process. We, however, continued to treat the condition conservatively.

On November 8, 1935, 30 days after the accident, the traction was removed and we were surprised to find that the boy could use his arm perfectly. A roentgenogram taken 30 days later showed a bridge of new bone forming between the distal end of the proximal fragment and the acromion process (Fig. 2). Measurements of the lengths of the clavicle on both sides showed a shortening of only one centimeter on the left side. The boy was discharged December 23, 1935, at which time the new bone forming the distal half of the clavicle had become dense and signs of erosion of the old fragment could be clearly seen in roentgenograms. Since then this erosion has continued and the size of the loose fragment is but one-third of what it was originally (Fig. 3). There seems no doubt that in a year's time this fragment will have entirely disappeared. Meanwhile the fracture of the glenoid fossa had completely healed without deformity, but in a recent roentgenogram an opening or hiatus is seen in the body of the scapula.

The boy now has normal function, and measurements show no shortening of the bone. Palpation of the clavicle reveals a mass extending into the supraclavicular fossa which is caused by the formation of new bone beneath the periosteum, which was raised up in a ridge by the displacement of the fragment.

---

* Presented before the New York Surgical Society, May 13, 1936. Received for publication June 17, 1936.

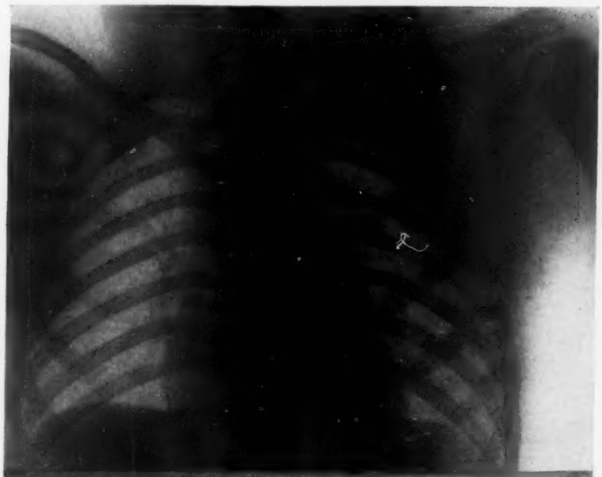

FIG. 1.—Roentgenogram showing a fracture-dislocation of the outer third of the clavicle and a fracture of the neck of the scapula.

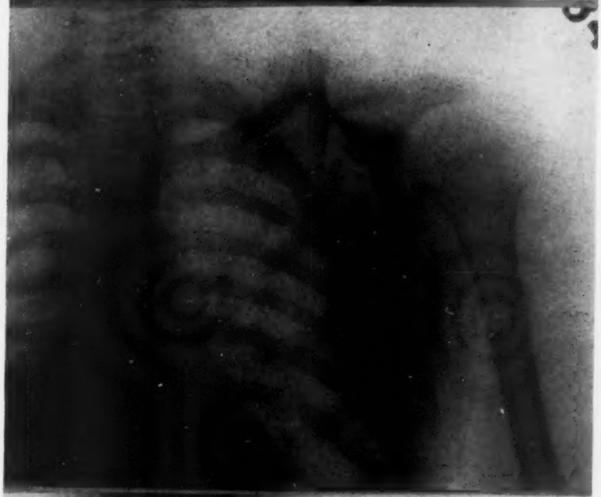

FIG. 2.—Roentgenogram showing the condition eight weeks after the accident. Note the formation of new bone between the inner fragment and the acromion process.

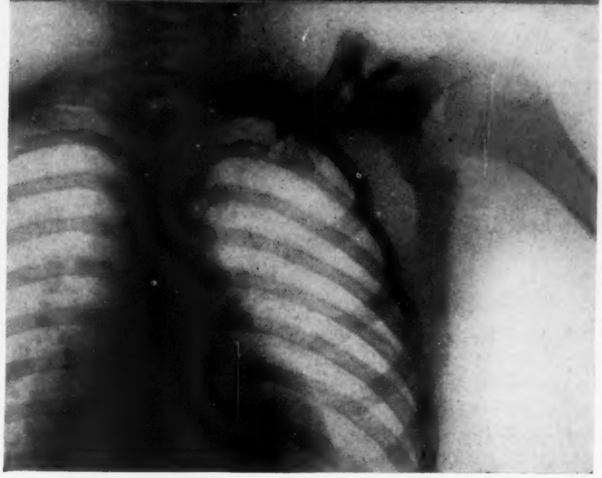

FIG. 3.—Roentgenogram showing the condition 28 weeks after the accident. A new clavicle has been formed. The displaced fragment is undergoing absorption.

Inquiry may be made as to what effect this accident may have had upon the growth of this bone. This to me was at first a question of some importance until it was recalled that the clavicle has but one epiphyseal cartilage which is situated at its sternal end.

I think this case demonstrates the power of a growing bone to replace loss in its continuity, and that in many cases a conservative course of treatment is wiser than the undertaking of a radical procedure, before it is known what nature may accomplish.

DISCUSSION.—DR. CARL G. BURDICK (New York) congratulated Doctor Beekman on his conservatism, adding that he and Doctor Beekman had had the opportunity of seeing a good many fractures in children and that while, every now and then, they were quite surprised at the final results in cases of marked displacement, he doubted if they had ever been more pleased than by the results obtained in this particular case. If one looks at the roentgenogram carefully, it is possible to see a bridge of periosteum along which the new bone is being laid down. He believed that eventually the displaced fragment would be absorbed. One sees quite often in supracondylar fractures of the elbow with a considerable posterior displacement, the bridge of periosteum between the displaced fragment and the shaft with new bone being laid down along it, followed by absorption of the displaced proximal fragment, generally with hardly any evidence of fracture at the end of two or three years. When one has observed many of these cases there is a tendency to become a little too conservative. It is important to appreciate the difference between fractures with considerable displacement of the shaft of the bone and fractures involving the joints. Comparing greenstick fractures, where there is a considerable amount of bowing, with fractures of both bones of the forearm with marked displacement and considerable overriding, one finds that cases of marked bowing take very much longer to correct themselves than do those where there is a complete fracture with considerable displacement and overriding.

DR. JOHN J. MOORHEAD (New York) referred to the possibility of there being shortening on account of involvement of the epiphysis. Contrary to the general belief, he said that it is very difficult to recall a case of long bone fracture in a child in which, even with considerable involvement of the epiphysis, there had been lasting changes. In trying to review these, as Doctor Beekman presented his case, Doctor Moorhead said the only cases he could think of in which ultimate function is lacking is in fracture of the lower end of the femur, in which one is much more likely to have epiphyseal changes than in any of the other bones.

DR. CLAY RAY MURRAY (New York) emphasized the benefits of conservative treatment in fractures in children. Regarding the question of whether permanent damage is or is not rare in epiphyseal injuries, he said that he had had occasion to see epiphyseal separation result in permanent damage. In a recent careful follow up at Presbyterian Hospital, it was found that between 4 per cent and 5 per cent of cases with an epiphyseal separation showed damage with deformity, and that while approximately 75 per cent of these, after a period of years, were normal, 25 per cent—or 1 per cent of all epiphyseal separations—showed permanent deformity requiring operative intervention.

Dr. Fenwick Beekman (New York) in closing said that the healing of fractures in children is quite different from that of fractures in the adult. The periosteal tube is a very important factor in the production of a new shaft. Some years ago he presented before the New York Surgical Society a supracondylar fracture with a great amount of displacement of the lower fragment in which a new shaft was being formed to connect up with the displaced epiphysis of the humerus, while the old shaft was being absorbed. That child did not have full function until two years after the injury because of the presence of the old shaft. Of course, the epiphyseal side is the site where, in all probability, the proliferation of cartilage cells occurs. Therefore fractures that cut across epiphyseal cartilage are those in which we most often find interference with growth, and where a fracture does involve the epiphyseal cartilage one should always give a poor prognosis. In those which do not involve it there is no danger whatever of interference with growth. Regarding epiphyseal injuries, Doctor Beekman said that he has had the opportunity to see a large number of fractures, in which the fracture line was not shown in the film, but where the cartilage of the epiphysis has been injured together with injury of the capitulum or the trochlear, and the proliferating cells were involved, yet when these children were discharged from the hospital there was no deformity. However, many returned after four or five years with marked valgus or varus deformities, due to damage of the trochlear or capitulum growth centers; this is also true of certain cases of separation of the lower epiphysis of the radius, but in these cases one can see the fracture line running across the epiphyseal cartilage. Doctor Beekman said he was very much opposed to operation upon dislocations of the epiphysis of the lower end of the radius, for the simple reason that they all straighten out if one gives them time. On the other hand, if one goes in with his chisel he may injure the proliferating cells of that plate. Regarding the possibility of shortening in the case presented, when the boy left the hospital he had less than 1 cm. shortening. When examined one week ago, this had been diminished to less than .5 cm. and this will probably not increase. In fact, the epiphyseal cartilage plate at the sternal end may be stimulated so that eventually this injured side may actually be longer than the other.

HIGH INTESTINAL FISTULA

A METHOD OF TREATMENT

Joseph Tenopyr, M.D., and Benjamin Shafiroff, M.D.
Brooklyn, N. Y.

FROM THE SURGICAL SERVICES OF THE KINGS COUNTY AND CALEDONIAN HOSPITALS, BROOKLYN, N. Y.

The management of a duodenocutaneous fistula or any other type of high intestinal fistula requires the surgeon's best effort. There are two serious complications that must be guarded against. One is the resultant alkalosis or acidosis depending upon the location of the fistula and associated with the loss of salts in body fluids. Such loss unless replaced continuously by physiologic solutions leads to death. The second complication is a severe excoriation of the skin and deeper structures of the anterior abdominal wall by the intestinal juices.

Submitted for publication July 18, 1936.

This skin reaction is of a chemico-inflammatory type characterized by erosions terminating in slough. The phenomenon is due to enzymic digestion and may or may not be accompanied by bacterial contamination. Co-Tui[1] has demonstrated on a qualitative and quantitative basis that all skin excoriations of surgically produced intestinal fistulae are due to tryptic digestion varying in concentration in the fistular discharge from 200 trypsin units (sigmoidostomy) to 2,000 trypain units (cecostomy). The higher the location of the fistula the greater the loss of intestinal enzymes, and the more marked the effect on the skin surface.

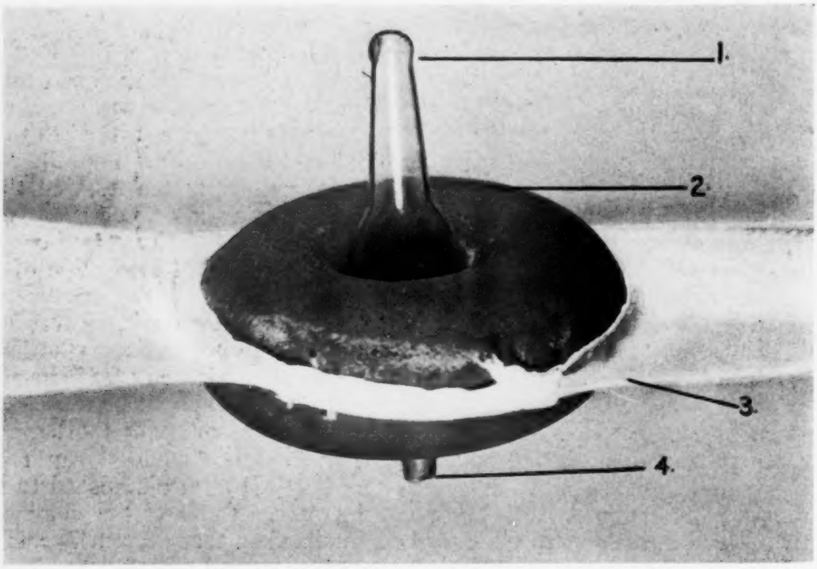

FIG. 1.—Close-range view of fistula belt. (1) End of Murphy drip tube for attachment to suction. (2) Rubber pessary ring. (3) Moleskin bandage sewed around rubber ring. (4) End of Murphy tube which fits into fistulous stoma.

A high cutaneous fistula occurs usually after surgery upon the stomach, duodenum, or jejunum. With the increase of plastic surgical procedures on the gastro-intestinal tract, the incidence of fistula has increased. The latter complication becomes apparent usually after the fourth postoperative day, and is due to leakage from the intestinal suture line, unnoticed trauma to intestinal tissue from pressure clamp or fistulization from improperly located drain. Immediate surgical repair by direct suture or sidetracking anastomosis is never indicated because of the high mortality (50 per cent) directly related to the patient's poor general condition.

Conservative therapy offers the best prognosis. Appended is a brief review of the various efforts directed to prevent the skin excoriations, which, if not controlled, assume vast proportions and may quickly involve the entire abdominal wall. The type of treatment of a fistula may be either mechanical or chemical. The chemical methods are usually of three types. Potter[2] recommends a beef preparation which is placed about the stoma of the fistula and encloses decinormal hydrochloric acid introduced directly into the opening of the sinus. Co-Tui[3] popularized the use of kaolin, which is a colloidal absorbent, for the electronegative trypsin. Various methods for the irrigation of the area about the cutaneous fistula with antacids or antalkalis, to inactivate the ectopic enzyme, are also recommended. The mechanical methods consist principally of the removal of the fistular contents by means of suction (Cameron,[4] Lahey[5]). Einhorn recommends the passage of a duodenal tube beyond the opening of the fistula with feeding by this method. Others have tried to plug the external opening of the sinus and have met with varying degrees of success.

We report a method of treating high intestinal fistulae which embraces both mechanical and chemical means. We find that chemical methods alone without suction are inadequate. The device described has been used successfully on four cases.

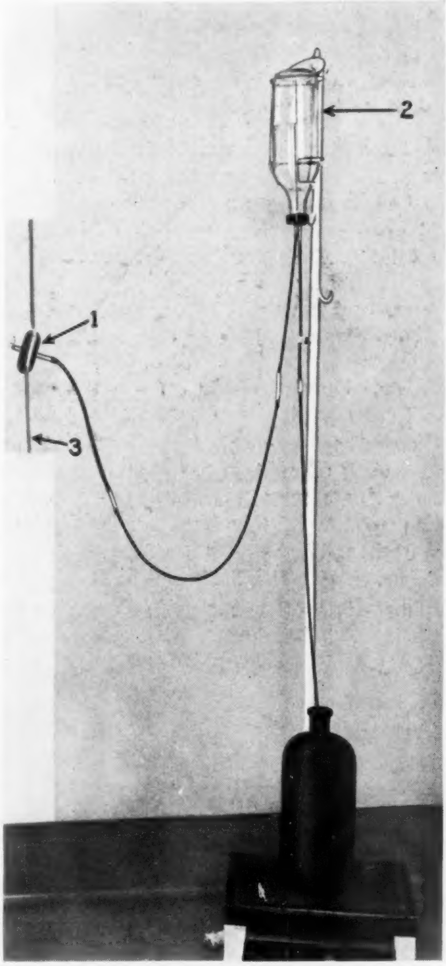

FIG. 2.—Showing fistula belt attached to suction ready to be applied. (1) Rubber pessary ring containing Murphy drip tube. (2) Wangensteen suction. (3) Moleskin belt sewed onto rubber ring.

ILLUSTRATIVE CASE REPORT

Patient J. H.—On the fifth day following a plastic gastro-intestinal repair for duodenal ulcer, a discharge was noted on the dressing. This was at first believed to be a simple wound exudate but proved to be intestinal juice, and the existence of a fistula was appreciated. Direct plugging of the fistula failed. Potter's beef preparation did not seem to restrict the excoriation which was rapidly spreading. The patient's condition was precarious. It was estimated that he lost from one to three liters daily of intestinal juices through the fistula. Continuous intravenous infusion barely replaced the fluid loss. Though an intern was detailed solely for the management of this case, the excoriations progressed, involving the entire surface of the abdomen and were extending up onto the chest wall. Five pounds of kaolin were used daily for dressings which were changed hourly but which proved quite inefficacious. Suction as obtained from the usual operating room electric apparatus was not feasible because of the pain evidently caused by excessive suction pulling on the intestine.

The following apparatus was finally elaborated. It consisted of a Wangensteen suction which seemed to give "physiological" suction and at no time caused pain. A soft rubber pessary, which resembles a doughnut in appearance (Fig. 1.) was placed about the fistular opening. To its side was sewn muslin bandage, or adhesive was attached. The belt was fixed by tying it around the patient's back. The hole of the pessary lay directly above and coincided with the stoma of the fistula. Tightly fitted into the pessary was a Murphy drip glass cannula, the tip of which just dipped into the fistula about a centimeter below the skin surface. The outer end of the cannula was connected to the Wangensteen suction (Fig. 2). About the large circumference of the pessary a small amount of koalin was heaped. This method worked satisfactorily. It was in continuous use for three weeks. The progressive erosion of the skin ceased and spontaneous healing ensued. After a week, the patient was allowed food by mouth. It was interesting to see him start the action of the suction by opening the valve of the Wangensteen tube whenever he felt the escape of juices onto the skin; or stop the suction when he felt dry. The sinus closed spontaneously.

SUMMARY

(1) A simple method, combining the advantages of mechanical and chemical means, for the prevention of skin excoriation, and the closure treatment of high intestinal fistulae, is reported.

(2) It has been satisfactorily employed in four cases.

REFERENCES

[1] Co-Tui, F.: Excoriations Around External Gastro-Intestinal Fistulae. ANNALS OF SURGERY, **98**, 242, 1933.

[2] Potter, C.: Treatment of Duodenal Fistulae. J.A.M.A., **88**, 899, March 19, 1927.

[3] Co-Tui, F.: Kaolin in the Treatment of External Gastro-Intestinal Fistulae. ANNALS OF SURGERY, **91**, 123, 1930.

[4] Cameron, A. L.: The Treatment of Duodenal Fistula. Surg., Gynec. and Obstet., **37**, 599, 1923.

[5] Lahey, F. H.: The Treatment of Duodenal Fistulae by Suction. Surg. Clin. N. Amer., **4**, 1489, 1924.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D.
1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa.